

Comments on California Air Resources Board Report:

Draft Technical Support Document for the
“Proposed Identification of Environmental Tobacco Smoke as a Toxic Air Contaminant”

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SUMMARY COMMENTS

The new report on the “Proposed Identification of Environmental Tobacco Smoke as a Toxic Air Contaminant” is an attempt at a thorough review of new scientific literature with regard to emissions of, exposures to, and health effects from environmental tobacco smoke (ETS). In some sections and subsections, the report provides a solid analysis. However, in general, the Draft Report is woefully inadequate, and needs substantial revisions before it should become a matter of record. After reviewing the document, I have three major criticisms of and concerns about the document.

First, for its analysis of exposures of Californians to ETS, it relies too heavily on indirect indicators of exposure to ETS and its components, such as time spent around smokers, and employs examples of potential exposure scenarios, and attempts to model exposures from such, instead of using data available from the scientific literature that measures exposures directly. In addition, after having used surrogate measures of exposure, there is no attempt made in the Report to confirm the accuracy of predictions by using previously published data.

Secondly, there is no perspective provided in the report. For a government agency to release such a document without providing perspective that the public can use to interpret the data is unconscionable. For example, much is made of the emissions of certain components, such as carbon monoxide, from cigarettes. While 1907 tons per year of CO may sound like a lot, in fact, it is the equivalent amount of CO emitted from a few thousand of California’s millions and millions of automobiles and heavy vehicles. To seek to regulate smoking in the basis of emissions into the ambient environment would appear ludicrous at best, and threatens the credibility of the entire Report.

Third, evidence is provided in the report to indicate that the constituents of ETS begin to react and decompose within short periods of time following their emission into the ambient environment. Clearly, ETS in ambient air in sunlight for any important length of time is no longer ETS. And yet the Report provides no justification or rationale as to why the use of existing regulations that establish safe concentrations of many of the components on interest in ETS is not an appropriate approach. ETS is treated like some sort of nefarious elixir that lasts forever, and yet the data provided in Section VI shows that this is clearly not the case. That such is not presented provides the perception that the authors of the report are biased and have other agendas beyond the examination of ETS as a toxic air pollutant.

Finally, perhaps the most egregious transgression of the Draft Report is that of its clearly incomplete and sometimes biased reviews of the scientific literature. This bias leads to statements that are simply unsupported by the scientific literature and provides for an unwarranted tone of “advocacy” that threatens the entire credibility of the draft report. That the Draft Report selectively ignores key scientific studies, or spends pages discussing criticisms of only selected studies, while ignoring criticisms of other similar studies provides for a sense of bias on the part of the authors of the Report. If these errors are permitted to stand in the final document, the report is likely to be dismissed by anyone who is not an anti-smoking activist.

Specific comments on Sections.

Chapter 3 Chemical and Physical Properties of ETS

This is a reasonably succinct summary of major properties of the complex mixture known as ETS. There are some errors and mis-interpretations that need to be corrected.

Page III-2,

The statement: “With few exceptions (e.g., hydrogen cyanide and organic acids), sidestream smoke contains greater mass emissions as compared to mainstream smoke (Jenkins et al., 2000) on a per cigarette basis.....” requires some additional explanation. The reason why SS smoke contains more material typically is because greater mass of tobacco is consumed during smoldering, compared with active puffing. However, many of the more basic components exist in even greater relative concentrations because combustion conditions (air flow and fuel consumption rate) favor the production of more basic species.

Page III-3

In the top paragraph, the text fails to make clear that most of the mainstream smoke that contributes to ETS is exhaled mainstream, that has been diluted in the lungs of the smoker, aged, and scrubbed of some of its more soluble gas components.

Page III-4

Last Paragraph The monograph to which the citation Jenkins et al, 2000 refers did not involve any new experimental work. No measurements were made.

Page III-5

First Paragraph: The statement “In general, highly concentrated mainstream smoke has constituents preferentially distributed in the particle phase region (Jenkins et al., 2000). Smaller sidestream smoke particles in the ambient air can be inhaled deeply into the lower respiratory tract, where they can have a deleterious health effect.....” suggests a nearly binary distribution of tobacco smoke droplets (particles) between SS and MS smoke. However, given the huge breadth of the distribution, the distributions of both smokes should be considered as continuums. *Also, the suggestion that somehow the slightly smaller particle size distribution of SS may result in more deleterious health effects is not supported in the scientific literature.* While there may be differences that are statistically different in the distribution parameters, such as the mass median aerodynamic diameter, it is not altogether clear that there is a true functional difference in the two distributions. If there is new evidence of this, then the authors need to cite such.

Chapter IV Production, Uses, Sources, Emissions, And Smoking Trends

In the discussion of emissions of cigars and cigarettes, there is a serious lack of perspective provided to the reader to evaluate the relative importance of the emission.

Page IV-2

Last Paragraph The work described in Djordjevic et al (2000) represents an important contribution to the scientific literature, but it is unclear how a discussion of the carbon monoxide in *mainstream cigarette smoke* bears on the discussion of ETS emissions. This is particularly true for CO, virtually all of which is scrubbed from MS smoke once it is held in the smoker’s lungs for a few seconds.

Page IV-7

Table IV-3 presents a summation of estimates of statewide emissions of three components of environmental tobacco smoke, respirable suspended particulate matter, nicotine and carbon monoxide.

The lack of any data comparing this to the same emissions from other sources is a serious flaw in the report, since no perspective is provided for the reader. For example, how do these CO emissions compare with those of the motor vehicles in the state? According to the EPA, each typical automobile emits 575 pounds per year of CO. So it would take less than 7000 cars to emit the same amount of CO that all the smokers emit in California. Compared to the 15 million or so cars in the State, such a trivial comparison threatens to undermine the potential importance of a report such as this. In terms of nicotine, no comparative data is provided. California has a major agricultural industry. Nicotine is present in the flesh of tomatoes, peppers, eggplant, and all the vegetables of the solanaceous family. The amount of nicotine that is emitted by all crops is not provided so that the reader can have some perspective. The levels of RSP that are emitted by the smoking of cigarettes, something like 365 tons per year, seems pretty insignificant compared to other sources across the State. The report needs to provide data with respect to power plant emissions, emissions from vehicular traffic, including releases of RSP from the wearing of break linings and exhaust systems, and the agricultural business within California. Without such data, the report loses much of the respect that it should have, and appears to be unnecessarily advocative.

Furthermore, the report is unclear as to how the emission levels were calculated. When asked about this in the March 15, 2004 review of the Draft Report, the team responsible indicated that the emissions were calculated assuming that all the cigarettes smoked in California would contribute to ambient levels of air pollutants. For this assumption to be rational, either all cigarettes smoked in California would have to be smoked outdoors, or all of the components of smoke generated indoors would have to find their way to ambient air with no losses, either through reaction or deposition on inside surfaces. Since neither of these assumptions are rational, the estimate needs to be corrected for realistic circumstances. Otherwise, this calculation will have no credibility.

Chapter 5 Exposure to Environmental Tobacco Smoke

The manner in which the Chapter is written gives the appearance of placing greater reliance on modeling studies of exposure, rather than relying on direct measurement of exposure. If there was no data as to personal exposure to ETS, such might be understandable. However, such is clearly not the case. However, the Report ignores key available data that is California-specific, and appears to cherry-pick studies for inclusion without substantial, factual information as to why certain studies were ignored. The Chapter appears to place a great deal of reliance on modeling studies conducted in single environments that have been manipulated, and gives lesser weight to studies of measured personal exposure.

Page V-4

There is a discussion as to “exposure to smokers” by considering the time spent around smokers. However, no data is presented to support the contention that time spent around smokers, or the detection by the human that they have been exposed to ETS, results in exposures that are relevant from a clinical or health standpoint. Based on what we know about dispersion of gaseous molecules, one can make the argument that everyone in the state is “exposed” to some of the molecules of ETS 24 hours per day, seven days per week. In many cases, it may be difficult to measure, because the concentrations of the molecules would be so small. However, everyone IS exposed.

The Report fails to mention the fact at this point that strictly speaking, “exposure” is the product of time and concentration of material to which one is exposed. To discuss “time” of exposure only addresses one half of the exposure equation. Whether or not an individual is “exposed” is really irrelevant. The more important question is: how many individuals have exposures (the products of concentration and time) that are clinically significant? Let me draw from a personal example. I typically jog through our

neighborhood about 5 – 6 days per week. Since I jog in the early evening, there are a fair number of vehicles that pass me on the streets. I have a pretty sensitive olfactory system, and I can smell tobacco smoke at pretty low levels. In fact, I can smell it when smokers drive by in their cars, even with the windows rolled up. OK, if I can smell it, I KNOW I am getting exposed. However, is there a single physician willing to get up and say that such an exposure is truly damaging to my health, or even the cumulative effect of all the exposures I have received in the 15 years of jogging in this subdivision has any sort of clinical significance? ***To simply say that a person is exposed provides no useful information, because no perspective on the degree of exposure is provided.***

Page V6

The comment is made that solanesol can not be a good marker for ETS outdoors because it degrades in sunlight. Well, so do many other ETS constituents. Based on National Academy of Sciences criteria for good markers, it would sound like solanesol would do a good job tracking those constituents that degrade in sunlight. Also, it is true that solanesol levels can be low, but one can adjust sampling times or sample collection flow rates to compensate for such. It is true that there are no good commercially available standards for 3-EP. However, under standard protocols for analysis of nicotine and 3-EP, 4-EP elutes at essentially the same time and has been used by several laboratories for a standard.

Page V7

The new CARB study is introduced. However, the study appears to focus solely on nicotine, and as such, is subject to the limitations of this marker, which are not acknowledged in the material provided. Also, very high flows are used for sampling through large XAD-4 cartridges. Has this sampling approach been validated? Clearly, the fact that ***this study has not been reported in the peer-reviewed scientific literature*** needs to be acknowledged so that readers and scientists can weight its value accordingly, relative to the host of other exposure studies that have been through peer-review.

Also, several peer-reviewed studies have clearly demonstrated that because of its highly absorptive nature, nicotine can remain in the air hours or days after smoking has ceased. It does not appear that the Report acknowledges this limitation of nicotine as a marker.

Page V-9

Given the discussion in Chapter VI (see below), that acknowledges the degree of dilution/dispersion of ETS, interaction with UV light and other contaminants, discussion of “ETS” in ambient air, after a significant amount of time has passed, seems incongruent with the findings of Chapter 6. The authors of the Report present no supporting data to indicate that ETS survives with most of its primary constituents intact for any length of time. Such provides the serious impression on the part of the reader that “one hand does not know what the other is doing” in this Report. As such, such an inconsistency threatens the credibility of the entire Report.

Also, the Report begins a discussion of modeling of ETS concentrations in different scenarios. Modeling can be a useful approach in the absence of direct measurements. However, direct measurements are straightforward to conduct, and modeling can suffer from focus on one or two experiments and over-extrapolation of the data.

Page V-10

Near the bottom of the page, the statement is made that other sources of RSP contribute much less to indoor levels of RSP than does ETS. However, no data is cited to support this claim, except ANOTHER

CARB report on ETS. In addition, the comment ignores the wealth of scientific, peer-reviewed data which indicates that for most exposures of humans, in all but the most tobacco-smoke polluted environments, ETS contributes substantially less than half of the RSP. (See Jenkins et al, 2000, cited in the Report.) It is easy to determine the relative contribution of ETS if one measures solanesol levels in indoor air.

Page V-13

I believe it is here that the report performs an analysis of ETS concentration measurements in indoor air in California and elsewhere. Interestingly, the report ignores the data obtained from the so-called 16 Cities Study (Jenkins et al, 1996) in which Fresno, *a California city*, was one of the Cities in which monitoring was conducted. The data has been available for the entire study, segregatable by city, for years through the Sapphire Group (eg. Graves et al, 2000), and yet, the authors of this report chose to ignore this key piece of data. For example, 55 subjects in Fresno reported being exposed to the smoke of 1 or more cigarettes. Respirable suspended particulate matter (RSP) 24 hour time weighted average (TWA) concentrations ranged from 3.9 – 190.1 $\mu\text{g}/\text{m}^3$. 24-hr TWA nicotine levels ranged from 0.0 – 5.66 $\mu\text{g}/\text{m}^3$. To ignore such relevant data in the Report is inexcusable.

Page V-16

Why the authors would use the Graves et al (2000) manuscript to summarize the results of the so-called 16 Cities Study (Jenkins et al, 1996), when the Graves study focuses on *non-smoking* workplaces, is not justified in the text. Why not cite to the original study (Jenkins et al, 1996), that segregates data according to both smoking and non-smoking workplaces, or the derivative manuscript that specifically focuses on data analysis of workplace exposures (Jenkins and Counts, 1999)? Also, focusing on the Graves et al (2000) data presentation results in a data analysis that is grossly in error, and such errors give the impression of biased data analysis, which detracts from the entire report. For example, a claim in the Report is made that “ ... results are somewhat low relative to other similar studies” However, no supporting data is provided to substantiate the claim. In fact, the comparison of mean 16 hour TWA away from work levels in smoking homes for RSP and nicotine for the 16 Cities Study (Jenkins et al, 1996), 44 and 2.71 $\mu\text{g}/\text{m}^3$, respectively, compares quite closely to that reported by Leaderer and Hammond (1991) of 44.1 and 2.17 $\mu\text{g}/\text{m}^3$.

Secondly, the Report indicates that demographics unrepresentative of the US population are responsible for lower exposure concentration levels. However, the Report fails to cite any other manuscripts where demographic data was reported for the subjects and fails to criticize any other studies, such as the aforementioned Leader and Hammond work, for skew demographics. (In the case of the Leader and Hammond 1991 manuscript, all the data was obtained from 47 homes in two counties in New York State.) The report fails to cite any other manuscript in the scientific literature that reports direct personal exposure to ETS that achieved a truly demographically representative sample of the US population. Such biased data analysis provides an unnecessarily advocative tone to the Report. In addition, the 16 Cities Study is criticized for having a *lower population of smokers* than the US population at large. And yet the study is clear that it only focused on non-smokers and that smokers were specifically excluded from the population studied. The authors of the CARB report need to clarify their statements.

Page V-17, Table V-6

This table completely ignores several important studies, including *14* from Keith Phillips’ team at Covance Laboratories (see references), Sterling et al, (1996), Trout et al, (1998), Maskarinec et al, (2000),

Jenkins et al, (2001). Such omissions gives the perception, incorrectly or otherwise, that the authors of the report are “cherry-picking” the data that they are providing to decision makers.

Page V-22

In the discussion of RSP studies performed in California, the Report has ignored again the publicly available data on Fresno produced from the 16 cities Study (Jenkins et al, 1996). For example, for 27 Fresno subjects in truly smoking homes, RSP exposures ranged from 40 – 3324 $\mu\text{g-hr/m}^3$. Additional data is provided on ultraviolet absorbing particulate matter (UVPM) and fluorescing particulate matter (FPM) as markers for combustion derived particles, and solanesol-derived particulate matter (Sol-PM) as a marker for tobacco derived particulate matter.

Page V-23

In a discussion of studies of RSP outside California, the Report devotes an entire paragraph to an unpublished, un-peer reviewed study reported on James Repace’s web site. This study employed a nephelometer (MIE Personal DataRam (pDR)1200) for analysis of RSP concentrations. However, the Repace report ignores a body of data in the scientific literature that indicates that such nephelometers over-report actual concentrations. Indeed, in a recently published peer-reviewed manuscript (Jenkins et al, 2004), the pDR has been shown to over-report the concentration of ETS RSP by a factor of 2. That the CARB Report does not mention the lack of disclosure of over-reporting illustrates the problem of over-reliance on non-peer reviewed data. It also detracts from the potential credibility of the entire report.

Page V-24

Table V-8 This table ignores several other published studies (Phillips et al, etc). In addition, it cites the Graves et al (2000) manuscript from the 16 Cities Study, (that focuses on non-smoking workplaces) and references its UVPM data, when RSP data is cited in the original study (Jenkins et al, 1996).

Page V-27

In the discussion of other ETS constituents, all of the literature on levels of 3-ethenyl pyridine seems to have been ignored. For California, this would include the Fresno data from the 16 Cities Study, and for elsewhere, would include both the series of studies from Phillips et al, Georgiadis et al (2001) on ETS and PAH’s, and the work by Heavner et al (1996) on VOC’s in homes. Instead, the Report focuses on an unpublished, non-peer reviewed study by Repace.

Page V-30

Modeling Studies

There is too much reliance on the use of the term: “exposed” to ETS. The criteria for what constitutes exposure is not adequately defined in this part of the report, and yet there is clearly a huge range of potential exposure magnitudes from a given observation. For example, suppose two individuals report “exposure” to the smoke of one cigarette. One of them lives in a small house trailer with a spouse, while the other walks past a smoker as he enters an airport. Both of these individuals have been “exposed.” But the true exposures (ie, the product of concentration and duration) of the two individuals may vary by a factor of 100 or more. Frankly, to use the term “exposed” without reporting other factors is both potentially misleading and certainly obfuscativ.

Modeling studies should only be relied upon where there is an absence of personal exposure data from which to draw. The statement cited by the report regarding the amount of acrolein inhaled by the US population annually is so bizarre and off-target as to be embarrassing that the Report authors chose to include it. It may be that Americans inhale a total of 260 kg of acrolein per year, but they also eat something on the order of 7 billion kg of fat per year. This sort of statement provides the perception that the Report is unnecessarily advocative.

Page V-31

The discussion of a National Ambient Air Quality Standard applied to this issue seems inappropriate, since the air in at least 50 % of private residences would violate such a standard routinely, even if no smoking was occurring.

Also, in the modeling discussions, there is no comparison made to direct measurements of either concentration or exposure. That is not to say that models can not be accurate. It is just that some effort needs to be made to compare with real data where available. For example, an analysis of data obtained in the 16 Cities Study for Fresno, CA for subjects living in homes where cigarettes were observed to have been smoked, median 15.5 hour personal exposure TWA concentrations for RSP were $21 \mu\text{g}/\text{m}^3$, and the 80th percentile value was $42.2 \mu\text{g}/\text{m}^3$. 95th percentile value was $88.3 \mu\text{g}/\text{m}^3$.

The Repace presentation at the 2000 ISEA meeting is cited. Such is fine. However, if presentations are to be cited in this document that have not been published in the peer-reviewed scientific literature, then a) they need to be referenced in the text as such, and b) all presentations presented relevant to the subject matter must be cited and discussed. Many, many presentations relevant to ETS concentrations have been reported at scientific meetings in the last ten years, including the same meeting in which the aforementioned presentation was made, but their results have not been included in the data analysis. Such gives the perception that the authors of this section of the report are cherry picking the studies that provide results that suit whatever agenda they may have.

Summary of Indoor Data

Page V-33

The statement that RSP levels in offices and restaurants where smoking is permitted range from 100 – 400 $\mu\text{g}/\text{m}^3$ is not supported by any literature cited in the text (ie, there are no citations). Furthermore, it is incongruent with reported scientific literature. For example, in the work by Maskarinec et al (2000) cited in the Report, the median RSP concentration for non-bar areas in restaurants and bars was $66 \mu\text{g}/\text{m}^3$ and $82 \mu\text{g}/\text{m}^3$, respectively. 80th percentile levels of RSP were 117 and $228 \mu\text{g}/\text{m}^3$, respectively. In a manuscript not cited by the report, but clearly relevant (Jenkins et al, 2001), 72 samples acquired in 26 offices and cubicles in one large office building where smoking was unrestricted exhibited median and 80th percentile RSP concentrations of 29.9 and $46.1 \mu\text{g}/\text{m}^3$, respectively. Detailed thorough reviews of the scientific literature (eg, Jenkins et al, 2000) have usually demonstrated median or mean RSP levels in smoking offices to be less than $100 \mu\text{g}/\text{m}^3$.

Citations on this page are inadequate or confusing. For example, Repace (in press) is cited, but there is no citation in the list of references provided that a particular manuscript has been accepted for publication in a peer reviewed journal but not yet published. Ott, et al, 2003, is cited, but is not reported in the reference list. In addition, the work of Phillips et al, constituting a massive study of personal exposure to RSP is ignored, as is the work of the TEAM study.

The “estimate” of RSP levels in homes (presumably smoking homes, although this is not called out) ranging from 300 – 5,500 $\mu\text{g}/\text{m}^3$ is simply unsupported by the scientific literature. The authors of the Report need to support this claim clearly. In addition, to state that such estimates represent “the best concentration estimates for each microenvironment” borders on the preposterous, and acts to destroy the credibility of this Report.

Exposure Estimation Scenarios

At first blush, it may appear that providing a variety of exposure scenarios for representative situations might be a useful exercise. However, the devil is in the details, and for these cases, the details of exposure scenarios described suggest that such analyses have little basis in reality. Two examples are illustrative.

Consider Scenario C1, the Children’s Low Exposure Scenario. The only source of exposure that is calculated is for the child playing outdoors in an area that is adjacent to a neighboring business’s smoking area. As a surrogate for the concentrations to which the child is exposed, the authors of the report use the mean level of the outdoor smoking area outside a business. It should be noted that a) the CARB outdoor analysis (Appendix C) has not yet been reported in the peer-reviewed literature, nor is there any evidence that it has been accepted for publication. A review of the details in Appendix C reveals that, inexplicably, the investigators used an unconventional method for collection of ETS nicotine (sampling at 15 L per minute). There is no data provided to indicate that the methodology (either sampling or analysis) is comparable in performance to the widely accepted ASTM method for airborne nicotine (ASTM, 2001) nor whether the sampling and analysis method used has been reported in the scientific, peer reviewed literature. From what I can determine, it has not. (It should be noted that in a review of Appendix C, that discusses the analysis of the ambient air nicotine samples, I was unable to find any reference to the use of an internal standard for the GC/MS analysis of nicotine. If this proves to be the case, and the analytical lab really did employ an inherently non-quantitative technique (mass spectrometry) in an attempt to provide quantitative data without the use of an internal standard, the value of all the analytical results are called into question. It may be likely that the study would have to be repeated with better laboratory practices.)

Additional examination of the sampling scenario provides no data as to the actual size of the smoking areas. However, we do know that one of the samplers was placed on the edge of the smoking zone and a second sampler placed in the center of the area. Mean concentrations for the center and edge of the smoking area were used as a surrogate for the concentration to which a child playing in an area adjacent to the smoking area would be exposed. This strains credibility, since it would seem that, given the likely distance of the child in its play area from the actual smoking area and the likely dispersion of the ETS, the best concentrations to use would have been the **background** concentrations determined from the outdoor measurements. The child is not going to play in the middle of the smoking area, yet these are the concentrations that are used. This kind of scenario description severely diminishes the utility of the approach.

A second example is simpler. Scenario T1 is the Business Traveler scenario. This scenario includes a non-smoking business traveler standing outside an airport for one hour in a designated outdoor smoking area. It is extremely difficult to imagine how such would occur, realistically. A five-minute exposure duration might have been more credible.

These two examples suggest that the authors of the Report were seeking to boost exposure levels in these scenarios by using unrealistic situations. The authors need to revisit each scenario, and use both realistic concentrations (for example, background nicotine concentrations for the child) and realistic durations. Without doing this, the examples provided have no useful value, and damage the overall credibility of the report. Given the quality of the existing scenario, the statement on Page V-34 that a statewide analysis exposure estimate would be “less informative” than the examples provided is simply not true.

Section F Biological Markers of Exposure to ETS

Summary comments and concerns are as follows:

1. In many places, the review of the scientific literature is incomplete. Key data presentations have been ignored.
2. Criticism, either direct or thinly veiled, is leveled at some but not all of the studies. This provides an unnecessarily advocative tone to the Report, which seriously diminishes its credibility. If the authors believe that an analysis of the strengths and limitations of studies are useful to the discussion, then such an analysis must be performed on all of the studies considered for discussion.
3. No analysis was performed on the only California-specific data set available for personal exposure to nicotine and salivary cotinine levels, despite the fact that such data has been publicly available for years.
4. There is discussion of biomarker levels in smoking mothers, but no effort is made to rationalize its connection with the topic of section: biomarkers and ETS exposure.
5. There are no substantive conclusions for this section with regard to the stated objective (page V-50) to examine “the utility of biomarkers to assess the extent of exposure to ETS.” The “conclusion,” that cotinine in body fluids can be used to distinguish smokers from ETS exposed individuals, is hardly a quantitative assessment, and ignores key scientific findings in the area. These are a) overall indicators of exposure (number of cigarettes observed to have been smoked near subjects, smoking/non-smoking home/workplace classification groupings, etc, show proportional increases in cotinine levels for increasing nicotine exposure when data from individuals is composited into larger groupings. (This may be due to dampening of individual differences in metabolism.); b) individual cotinine levels, while having statistically significant correlations with nicotine exposure, appear to have little *quantitative* predictive capability (in other words, one cannot use cotinine level to quantitatively predict an individual’s exposure to within a factor of 2, or even 5); c) models based on metabolism of nicotine by smokers appear to be unable to quantitatively estimate the magnitude of inhaled dose of nicotine; and d) other biomarkers of tobacco specific constituents, such as tobacco specific nitrosamines, may ultimately be useful for qualitative or even semi-quantitative indicators of inhaled ETS dose. However, the analytical challenges of measuring extremely trace quantities of these markers in biological fluids are preclude their applicability to broad studies of ETS dose at this time.

Specific Comments:

Page V-54

The 16 Cities Study was not performed by LaKind et al. The 1999 manuscript is a further analysis of the data reported first (and conducted by) Jenkins et al, 1996.

If it is important to provide the reader with funding sponsorship or affiliation of authors, then full disclosure should be made for all authors cited: eg. Smith et al, 2005, well-recognized anti-smoking

advocates, reported Frankly, if the data have been reported in the peer reviewed literature, sponsorship or the personal preferences of the authors should not be considered in the analysis. Period.

Also, Dietrich Hoffmann's name is incorrectly spelled at the bottom of the page.

Page V-55

The statement that the EPA had raised a multitude of concerns (unspecified) regarding the 16 Cities Study in some post hearing commentary in February of 1996, when the peer-reviewed manuscript was not even published until December 1996, suggests that the authors are bending over backward to appear as advocates, rather than dispassionate, unbiased assessors of the scientific data.

Also, it should be noted that the 16 Cities Study reported personal exposures, and the work described in Hammond et al, 1999 are *area* concentrations of ETS nicotine. As such, the two data sets are not comparable.

Finally, the statement is made that personal exposure nicotine concentrations reported by Phillips et al (1998) in Prague are lower than in comparable studies. The reference to comparable studies is unclear. Do the author's mean compared to Phillips' other studies (most of which have, inexplicably, not been even cited by the report). Do the author's mean lower than the US 16 Cities Study? Whatever studies that are considered truly comparable to the Phillips work (large number of subjects, careful segregation of exposure types, breathing zone personal monitoring) need to be specifically cited here.

V-58

"The validity of workplace nicotine levels has been challenged..." Which workplace nicotine levels? Those reported by Phillips for Prague? If the authors want to critique individual studies, then the criticism needs to be spelled out and it needs to be done for all studies that are included in the data analysis. My suspicion is that the authors are referring to a criticism of the 16 Cities Study (Jenkins et al, 1996) published many months prior to the publication of the peer-reviewed manuscript. To include such comments without specifying the criticism gives a tone of apparent bias to the entire Report.

Also, despite the fact that the data from the 16 Cities Study for Fresno (nicotine exposure and salivary cotinine levels that could have been analyzed) has been available for years (see the last page of Graves et al, 2000, or http://www.ornl.gov/sci/csd/Research_areas/ecms_rd_etsce_16cities.html), the authors of the Report did not analyze that data.

Finally, the analysis by LaKind et al (1999) of salivary cotinine levels from the 16 Cities Study shows median salivary cotinine levels for subjects only exposed in the workplace (Cell 3, Table V-15) of 0.347 ng/mL. When corrected for typical differences between saliva and serum cotinine levels, the levels reported by Pirkle et al (1996) for subjects exposed only in the workplace would be 0.40 ng/mL. To report a criticism of the 16 Cities Study by EPA regarding workplace nicotine levels, and then have the actual cotinine values reported by two independent groups be nearly indistinguishable makes not sense. This sort of biased data presentation jeopardizes the credibility of the Report, and calls other conclusions by the authors of the Report into question.

Page V-59

The original data analysis of salivary cotinine and nicotine exposure from the US 16 Cities Study (Jenkins and Counts, 1999b) is not even cited in the references for the chapter. Also, the presentation of the cotinine data from NHANES III, reported in Pirkle, (1996), even though it is segregated such that it

would be directly comparable to that reported by LaKind et al (1999) is missing from this analysis. In addition, the whole body of Phillips' work (eg, Phillips et al, 1998, etc) is not referenced or discussed in the Report. This one page affords several examples of inadequate literature review, reporting and analysis of the applicable scientific literature for this Report. It would be easy for the reader to draw the conclusion that if *these* key studies are not considered, *other* key investigations in other parts of the report have been ignored.

Page V-65

The authors need to clarify the relevance of maternal smoking biomarkers to the topic being discussed in the Report. Such is not evident on this page.

Chapter 6 Atmospheric Persistence

The discussion in Chapter 6 is interesting. A considerable amount of data is presented to suggest that the lifetime of various components is, in some cases, is fairly short. However, there is little attempt to discuss the rationale of using outdoor air markers (such as the iso-alkanes or ante-isoalkanes) as long term markers for ETS in ambient air when many of the components of ETS have relatively short half lives outdoors. This apparent inconsistency needs to be addressed.

Page VI-1

The statement “.....Alternatively, as ETS ages, semi-volatile constituents of ETS, such as nicotine, may shift from particulate phase to the gaseous phase.....” seems to be incongruent with the latest scientific evidence regarding the state of nicotine in ETS. Most nicotine in fact is in the vapor phase of ETS (mainly emanating from sidestream smoke) as the ETS begins to form. A much better example of the shift from particle phase to vapor phase would be neophytadiene or n-C₂₇H₅₆.

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The data reported in Table VI-1 presents a large range of atmospheric lifetimes for known constituents of ETS. The reported range is 5 minutes to 12 days. Given this data, and the likely reactivity of many of the other constituents of interest, it seems very hard to make a case that what we refer to as “environmental tobacco smoke” is likely to maintain much of its character after a few tens of minutes in the outdoor air. Given such, one would have expected for the Report to provide some rationale as to why it is reasonable to consider ETS holistically as a toxic air contaminant. Such is missing from this report. Without a clear, strong justification as to why we should consider ETS as some sort of single entity, when it is clearly not such, it would seem that the pollution which results from ETS best be considered on a constituent by constituent basis. Many of the compounds of interest are already regulated under a variety of regulations. No compelling evidence is provided for the case that ETS survives as an entity and should be considered as such.

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