We are submitting the following comments on the first draft Integrated Science Assessment for Particulate Matter for consideration by the EPA Clean Air Science Advisory Committee

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Comments on EPA's First Draft External Integrated Science Assessment for Particulate Matter, EPA/600/R-08/139

By E-mail to: U.S. EPA

Docket ID No. EPA-HQ-ORD-2007-0517

Dear Sir or Madam:

ExxonMobil Biomedical Sciences, Inc. (EMBSI), on behalf of ExxonMobil, appreciates the opportunity to submit comments on the Environmental Protection Agency's (EPA or the Agency) First Draft External Integrated Science Assessment for Particulate Matter (ISA). ExxonMobil is an integrated oil company and major chemical producer in the United States. We therefore have considerable interest in, and will be impacted by, the manner in which the Agency reviews the National Ambient Air Quality Standard (NAAQS) for particulate matter (PM) based on the findings presented in the ISA.

The attachment provides detailed comments on the ISA. A summary follows.

Chapter 1: Introduction

As part of their last review of particulate matter, EPA prepared a list of new studies published since the completion of the Criteria Document (EPA, 2006a). The Administrator then considered the results of these studies in decision-making on the NAAQS in 2006 (EPA, 2006 b, c). Therefore, these studies do not constitute new scientific data for the current review. Notable examples include Laden et al. (2006), Jerrett et al. (2005), Sun et al. (2006), Dominici et al. (2006), Gauderman et al. (2004), and Kunzli et al. (2005). Chapter 1 should state that the studies included in the EPA 2006 compilation are not new studies since the last review of the PM NAAQS and that therefore they should not be used to support a change in the PM NAAQS.

Chapter 6: Integrated Health Effects of Short Term Exposure

6.1.1 Methodological Considerations

In this section, to help guide in the interpretation of human clinical studies, EPA has outlined the advantages and limitations of these studies. EPA has not, however, provided similar information to guide in the interpretation of observational epidemiology studies. We suggest including a section that reviews the advantages and limitations of time series and field observational epidemiology studies. In our detailed comments, we provide guidance for

identifying the key advantages and limitations that should be considered by EPA in evaluating such studies.

6.2 Cardiovascular and Systemic Effects

6.2.1 Heart Rate and Heart Rate Variability (pages 6-8 to 6-22)

EPA overstates the evidence that 1) exposure to ambient PM changes heart rate variability (HRV) and heart rate; 2) subtle acute and transient changes in HRV and heart rate, equivalent to those occurring in humans every day, have any biological significance; and 3) the effects on HRV and heart rate reported are specific to particulate matter less than 2.5 μ in size ($PM_{2.5}$) and not confounded by other correlated air pollutants for which EPA also asserts cause changes in HRV and heart rate. In our detailed comments, we include related background HRV and heart rate information that can guide the interpretation of studies using these endpoints. We recommend that EPA include this information in the ISA to assist the reader in evaluating the results and reconsider their conclusions on PM exposure and HRV and heart rate considering this related background information.

6.5 Mortality Associated with Short-Term Exposure

EPA concludes that the risk estimates for mortality for all causes for all ages range from 0.29% (Dominici et al. 2007) to 1.21% (Franklin et al. 2007) per 10 $\mu g/m^3$. This conclusion fails to capture the high degree of heterogeneity and uncertainty in the results of the new time series mortality studies, which if considered, would result in the true risk range extending to no risk or null.

We describe below the key uncertainties and sources of heterogeneity in the acute $PM_{2.5}$ mortality estimates. These comments are based on our critical review of the new data on the association between $PM_{2.5}$ and mortality. We recommend that EPA include these points in their conclusions. .

- Since the last PM standard review, only four new studies have become available that evaluated the association between $PM_{2.5}$ and mortality. Only one of these studies (Ostro et al. 2006) considered potential confounding by gaseous pollutants (e.g. ozone, NO_2, SO_2). We note that EPA also considers these gaseous pollutants to potentially cause acute mortality. The study by Ostro reported that inclusion of gaseous pollutants attenuated the mortality association for $PM_{2.5}$. Thus, since the last review, the relative importance of gaseous pollutants on mortality risk estimates for $PM_{2.5}$ remains unresolved.

- Since the last review, two studies (Ostro et al. 2006 and Dominci et al. 2007) critically evaluated the impact of various model specification factors on the $PM_{2.5}$ mortality association. The results indicated that the acute $PM_{2.5}$ mortality risk estimates are not robust to changes in time series model specifications. The factors influencing the $PM_{2.5}$ mortality association include the degrees of freedom used for smoothing time, the spline model selected for the regression, segmentation by season, and the lag times used.

- Since the last review, two studies (Dominci et al. 2007 and Ostro et al. 2006) evaluated the regional heterogeneity in the results of the $PM_{2.5}$ mortality association. Both studies reported significant and unexplained regional (Dominici et al. 2007) and county-wide

(Ostro et al. 2006) heterogeneity in $PM_{2.5}$ mortality risk, rendering any central or national estimate of acute mortality risk unreliable and misleading.

- Since the last review, no new studies evaluated the potential change in the $PM_{2.5}$ mortality association with reduced ambient levels of $PM_{2.5}$. However, one study is available that evaluated the change in PM_{10} levels (Dominic et al. 2007). The results of this study indicated that the risks attributed to a unit PM_{10} exposure (risk per 10 $\mu g/m^3$) decreased from the period 1994-1997 to the period 1995-2000 and that they were not statistically significant in the latter time period.

- Since the last review, there have been no new studies on the key issue of measurement error on $PM_{2.5}$ risk estimates. Thus, the information on the impact of measurement on $PM_{2.5}$ risk estimates in single pollutant models remains limited, and no information is available on the impact of measurement error in multi-pollutant models.

- Since the last review, a number of epidemiology, human clinical, and toxicology studies have evaluated PM chemistry that is important for health effects, including acute mortality. The results of these studies are variable and conflicting. They do not support a conclusion on which components of PM are most responsible for heath effects.

Chapter 7: Integrated Health Effect of Long Term Exposure

7.7 Mortality Associated with Long-Term Exposure

This section presents a seriously biased interpretation of the new literature. We recommend that EPA consider a new team of authors for this section.

The following points summarize our concerns. The attachment provides more detail.

- The ISA systematically introduces text and unsupported arguments intended to discount the results of any negative study (e.g., studies by Enstrom et al. (2005) and Lippfert et al. (2000)).

- The ISA discounts the paper by Janes et al. (2007a), which raises serious concerns about the methodology used in the key chronic air pollution epidemiology studies. This is done by selectively citing a letter-to-editor by Pope et al. (2007) that is critical of the Janes paper. Since the author of the ISA was a co-author of some of the key studies reviewed by Janes et al. (in particular the key American Cancer Society study), it appears that the author of the ISA is defending his own studies. The ISA then fails to cite the letter by Janes et al. (2007b) that responds to the criticism raised by Pope et al. (2007).

- The ISA systematically overlooks obvious concerns and limitations of some of the key new studies. Examples include:
    - failing to mention positive associations for non-hypothesized causes (e.g. accidents, digestive disorders) and potential confounding discussed in the key paper by Jerret et al. (2005);
    - selectively citing the full cohort analysis that reports positive associations while failing to cite the case control analysis that reports negative associations in the paper by Beelen et al. (2008);

- failing to mention the methodological flaw resulting in exaggerated risks in the paper by Miller et al. (2007) and failing to cite the letter-to-editor by Jerret et al. (2007) that describes the exaggerated risks; and
- failing to mention the serious methodological problems including lack of consideration of confounding pollutants, and concerns with the underlying data in the study by Laden et al. (2006).

Also, we strongly recommend deleting the reference to the Expert Elicitation (EE) effort on PM from the ISA (Roman et al., 2008). This effort, which was sponsored and administered by EPA, does not constitute "new scientific data." Rather, this work presents a collection of opinions from a group of scientists selected by the Agency. As described in our detailed comments, in our view the process used to select the experts and elicit these opinions was not objective. We disagree with the statement in the ISA that the EE can be used to support conclusions on the key uncertainties on concentration response functions for PM mortality. This statement should be deleted from the draft report.

Our view on the current status of EE is consistent with and supported by the recommendations of the National Research Council Committee on Improving Risk Assessment Approaches (CIRAA), a committee commissioned by EPA for the purpose of providing advice on improving risk assessment at EPA (NRC, 2008). In the chapter on uncertainty and variability, the CIRAA expresses serious concerns with both the methodology and use of EE. They do not endorse the use of EE in risk assessment.

Chapter 8: Public Health Impacts

8.1.1. Mortality Associated with Short Term Exposure to PM

This section does not present an objective summary of the literature. It cites only studies that support EPA's conclusion that there is no threshold for the health effects of PM. We recommend that the EPA include studies reporting thresholds, such as the study by Smith et al. (2000) that reports a threshold for $PM_{2.5}$ mortality in Phoenix, or the study by Nicolich and Gamble (1999) that reports a threshold for "total suspended particle" mortality in Philadelphia.

The summary of the study by Samoli et al. (2005) in the draft ISA fails to mention that the authors suggests a threshold model was reasonable. The summary also understates the high degree of city to city heterogeneity in the results. For example the concentration response functions for model cities London, Athens, and Crakov (Figure 1) are completely different from one another. There is also an unexplained regional difference. These findings should be added to the summary to provide a more complete picture of the results.

8.1.2. Mortality Associated with Long-Term Exposure to PM

This section fails to mention the study by Abrahomowitz et al. (2003) that examined the concentration response relationship in the key American Cancer Society data set using a flexible non-parametric modeling approach. Abrahomowitz et al. reported that levels of sulfate PM below 12 $\mu g/m^3$ had little impact on mortality suggesting a possible "*no effect threshold*." Failing to cite this key study compromises the transparency and credibility of this section.

8.1.3. Summary of Concentration-Response Relationship

EPA states that studies using various statistical methods have "consistently" found that the association between $PM_{2.5}$ and mortality in multi-city studies is adequately described by a no-threshold log-linear model. As mentioned above, the data on this topic are both limited and inconsistent. EPA should revise their conclusion, considering the following key points:

Short Term Mortality

- The large majority of studies examining the shape of the concentration response function for mortality have relied on Akaike Information Criteria and model fit criteria that were not developed to assess etiology theories and are therefore inappropriate for drawing conclusions on the nature of mortality concentration response function (HEI, 2003).

- The results of existing studies are inconsistent. Some studies report a log-linear relationship with no evidence for a threshold while other studies report the existence of thresholds. It is apparent that there are methodological differences that explain some of these discrepancies.

- In studies of multi-cities, there is a high degree of unexplained city-to-city heterogeneity in the mortality concentration response functions. The heterogeneity renders any central national estimate unreliable and of limited utility for risk assessment.

Long-Term Studies

There are only a few studies that have evaluated the shape of the concentration response function for chronic PM mortality. Thus, the assessment of risks for chronic PM mortality must reflect this degree of uncertainty and must present alternate approaches based on the assumption of a threshold.

In an examination of the key American Cancer Society study, a threshold for mortality was reported for one form of fine PM (sulfates), but the reverse relationship, i.e., steeper slope at lower concentrations, was reported for another form of fine PM ($PM_{2.5}$) (Abrahamowicz et al. 2003).

Results from the Expert Elicitation report (Roman et al, 2008) should be deleted. As mentioned in the attached comments, there are many methodological problems and biases evident in this report. The recent NRC report on improving risk assessment commissioned by EPA (NRC, 2008) concludes there is insufficient scientific data to support the use Expert Elicitation for decision-making.

In the update of the Harvard Six Cities Study (Laden et al.), the authors' claim of linearity was limited to the range study data. Thus, the model does not extend down to very low ambient levels. Further, we suggest the conclusions of Laden et al. regarding PM and mortality are inaccurate and should be modified. Plotting the data shows that the concentration-response functions are nonlinear for the complete follow-up and for Period 2. Thus the effect estimates from linear models overestimate risk, and graphical displays support a threshold or no association.

The effect estimate of 1.16 (1.07-1.26) in Laden et al. for the total follow-up is based on a linear model. This estimate is incorrect and overestimates risk as the relationship is not linear as readily observed when the data are plotted. Visual inspection suggests a threshold below 20 $\mu g/m^3$.

Concentration-response functions in Periods 1 and 2 are not comparable as the data are approximately linear in Period 1 and nonlinear in Period 2. This becomes apparent by connecting the data points in Figure 2 in Laden et al. The heterogeneity between Periods 1 and 2 is so great that it is not statistically valid to combine these results. The effect estimate of 1.13 in Period 2 is incorrect because it is based on a linear model and over-estimates risk for all cities except Harriman. There appears to be no association with PM in Period 2 since:

- None of the cities have significantly elevated effect estimates
- Three cities have effect estimates at or below 1.0 (one nearly significant) and
- The most polluted cities show decreasing risk as concentration increases (see Table 2 in Laden et al.).

In summary, the findings from Laden et al. (2006) do not support a mortality association in period 2, i.e., at current ambient levels in the six cities evaluated in this study. Therefore, the data from this study do not support the EPA recommendation to extrapolate mortality risks to very low levels using a log linear model.

If you have questions on this information, please contact me at 908 730-3417.

Sincerely,

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Attachment: Detailed Comments on the EPA 1st draft Integrated Science Assessment for Particulate Matter.

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