ANALYSIS OF A U.S. DEPARTMENT OF TRANSPORTATION REPORT ON AIRLINER CABIN AIR QUALITY (REPORT NO. DOT-P-15-89-5)

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This paper analyzes the section dealing with environmental tobacco smoke (ETS) in a recent study prepared for the Department of Transportation (DOT), Airliner Cabin Environment: Contaminant Measurements, Health Risks, and Mitigation Options (Report No. DOT-P-15-89-5; prepared under contract by GEOMET Technologies, Inc.).

In order for Congress to make reasoned policy decisions on complex issues such as whether exposure to ETS increases the risk of lung cancer, it must be able to rely on the accuracy and thoroughness of scientific analyses. We believe the DOT study requires comment by the scientific community because it is based on questionable data and assumptions, and ignores evidence from accepted methodological approaches to cancer risk analysis. These shortcomings undermine the conclusions of the report.

It does not serve the public health interest for DOT to present a study that takes into account only one side of an important scientific debate. Estimating whether ETS poses a health risk involves a great deal of uncertainty, and scientific opinions differ about how to deal with that uncertainty. However, presenting a worst case analysis based upon questionable data and unjustified assumptions, as was done in the DOT report, creates unnecessary anxiety about health risks and does not provide a sound basis for future health policy decisions.

Our main comments on the DOT report are summarized below. We have avoided highly technical arguments in the discussion that follows, but a list of references and an appendix are provided to assist readers who desire a more detailed understanding of the issues discussed in this paper.

Summary of comments:

1. ETS Exposure Measurement. Air quality measurements contained in the DOT report demonstrate that separating smokers and nonsmokers into separate seating areas aboard airliners yields extremely low ETS levels in the boundary seats closest to the smoking sections and virtually eliminates ETS exposure in the remainder of the nonsmoking section.

2. Cigarette Equivalent Dose. Using the method for calculating cigarette equivalents employed by the National Research Council (NRC, 1986), the DOT airline measurements indicate that a flight attendant who works only on international smoking flights (the highest possible exposure, according to this report) receives an ETS dose equivalent to smoking at most 1/2 of one cigarette per year.

3. Risk Estimates. The authors of the DOT report present two approaches to estimating possible ETS lung cancer risk, and they claim that their estimates are strengthened because the two methods yield comparable results. However, both approaches depend critically upon similar relative risk estimates derived from flawed ETS epidemiology studies. Further, the results of the DOT report are inconsistent with those of the dosimetric risk analysis approach, which yields far lower risk estimates.

Each of these points is discussed below in greater detail.

1. ETS Exposure Measurement

The data that were collected in the ETS exposure measurement phase of the DOT study appear to be reasonable given the technology currently available for obtaining ETS measurements under field conditions. It is noteworthy that the air quality measurements contained in the DOT report demonstrate that separating smokers and nonsmokers into separate seating areas aboard airliners yields extremely low ETS levels in the boundary seats closest to the smoking sections, and virtually eliminates ETS exposure in the remainder of the nonsmoking section. These data indicate that separating smokers and nonsmokers by three rows (referred to in the DOT report as the "boundary" section) eliminates all but the odor from exposure to ETS. There is zero ETS exposure, according to this report, for passengers or crew remaining in the nonsmoking section of airliners.

2. Cigarette Equivalent Dose

Using the National Research Council (NRC) method for calculating ETS dose (which yields the amount of "tar" deposited in the lung), and the respirable suspended particulate ("RSP") exposure data contained in the DOT report, the most highly exposed flight attendants (those working only on international flights) receive an ETS dose equivalent to 1/2 cigarette per year (See Appendix for this calculation). This dose estimate is comparable to ETS exposure estimates already reported for other environments by several authors (NRC, 1986, Table 5A; McAughey *et al.*, 1989; Lee, 1988; Arundel *et al.*, 1988).

3. Risk Estimates

The Geomet report presents two lung cancer risk calculations which rely on epidemiologic data on the association between ETS and lung cancer. This method

produces much higher risk estimates than an alternative dosimetric approach discussed at the end of this section.

The first risk assessment presented by Geomet uses a "phenomenological" model, first proposed by Repace and Lowrey (1985), which is based on the observation, reported by Phillips *et al.* (1980a, 1980b) that Seventh-Day Adventist (SDA) nonsmokers had lower rates of death from lung cancer and heart disease than did non-SDA nonsmokers.

The Phillips *et al.* study was exploratory, and hypothesis generating, in nature. The study looked at a wide range of health outcomes, but lacked many of the design and analysis features needed to test hypotheses. The SDAs are a unique population that differ from non-SDAs in many ways that could effect their health (e.g. dietary habits, alcohol consumption, education, occupation, income, race). Many of these lifestyle and demographic differences are recognized as risk factors for lung cancer. Among nonsmokers, such risk factors could account for the observed differences in lung cancer rates between the two groups.

Phillips *et al.* speculated about a number of possible hypotheses that could explain their data. One such speculation was that the difference in lung cancer rates among nonsmokers could be due to differences in ETS exposure. However no ETS exposure data were collected by the study, and no account was taken of other potential risk factors for lung cancer. The author's discussion about a possible lung cancer association was speculation, not a conclusion of the study.

Repace and Lowrey ignore the serious limitations of the Phillips *et al.* study and use the data from that study in an extraordinary way. They assume that the entire difference in observed lung cancer rates was caused solely by ETS exposure and proceed to create a dose-response relationship, in spite of the fact that there were no dose data. They do this by using exposure measurements of their own, taken in settings entirely

unrelated to the Phillips *et al.* cohorts. They then make a lengthy series of assumptions about the size and extent of exposure in the U.S. population to arrive at their lifetime risk calculation.

The phenomenological approach, then, rests squarely on an unjustifiable use of the Phillips *et al.* data, and an assumed dose-response relationship which was not based on exposure data for the study subjects. This model is generally regarded today as seriously flawed, and it is, therefore, surprising that Geomet uses this approach to ETS risk assessment. In a Staff Paper on the health effects of ETS exposure, the Office of Technology Assessment (1986) noted that it was inappropriate to assume, as Repace and Lowrey did, that the entire difference between the lung cancer death rates in the SDA and non-SDA groups of the Phillips *et al.* study was attributable to ETS exposure. The paper stated: "At best, one can conclude that *some part* of the difference between the two populations may be due to differences in passive smoking rates, but the assumption that it is reasonable to attribute the entire difference to passive smoking is unjustified. The effect of these and other flaws on the final estimates calls into question the reliability of [Repace and Lowrey's risk estimates]."

Several assumptions underlie the second risk analysis presented by Geomet, the "modified Armitage and Doll" approach, the most critical of which is the assumption that the relative risk of lung cancer for nonsmoking women with smoking husbands is approximately 1.3, and that this increased risk is due to ETS exposure. This relative risk is based on a "meta-analysis," or combination of results from, the ETS-lung cancer epidemiologic studies. As explained below there are serious questions about the validity of those studies and good reasons to believe that the elevated risks reported in some of them are the result of bias and confounding factors, rather than a real effect of ETS exposure on lung cancer incidence. A meta-analysis cannot remove the defects of the

individual studies; if observed associations are the result of bias, a meta-analysis merely provides spurious reinforcement of invalid results.

The Geomet report uses the relative risk of 1.3 and data on lung cancer incidence among nonsmoking women, together with estimates of RSP concentrations in households with smokers, to derive a "dose-response coefficient" from the multi-stage model of carcinogenesis (Armitage and Doll, 1954 and 1961). The model with this coefficient is then used to calculate risk estimates for crew and passengers exposed to ETS on commercial airline flights.

Although there are many uncertainties in this approach, the critical element, as noted above, is the assumption that nonsmoking women with smoking spouses have a lung cancer relative risk of 1.3, and that this relative risk reflects a causal association. Unless it can be definitely concluded that the associations reported in the epidemiologic studies on which the 1.3 relative risk estimate is based are causal and not artifactual, the risk estimates derived in the Geomet report from the multi-stage model have no validity.

In fact the studies of ETS and lung cancer suffer from methodological flaws in their design and execution which could introduce bias into the results. There is good reason to suppose that biases and confounding factors inflated the observed relative risks in many of these studies. Detailed discussions of these points are presented in the recent reviews of Layard (1990) and Lee (1989), and are summarized here:

1) The study results are weak and inconsistent, and thus do not offer convincing evidence that any observed association is not an artifact produced by bias or confounding factors. Dose-response relationships are nonexistent or negative in some studies, and none of the studies demonstrates a significant dose-response when attention is restricted to exposed subjects, which is a recommended procedure (Breslow and Day, 1987).

Further, some studies display contradictory results with respect to the lung cancer cell type for which risk elevation with exposure is observed.

2) The results of epidemiologic studies are subject to distortion by various types of bias, and in particular case- control studies are susceptible to selective recall bias, due to the propensity of cases to recall exposure more completely. None of the studies of ETS and lung cancer used objective ETS exposure measurements such as biologic or environmental markers. Another important source of bias in these studies is under-reporting of current or past smoking by professed "never-smokers." Such under-reporting would result in over-estimation of the relative risk, since the smoking habits of spouses, as well as smoking and lung cancer incidence, are positively correlated.

3) A number of studies have suggested an association between lung cancer and factors such as occupation, nutrition, and alcohol consumption. There is evidence that such factors are also correlated with ETS exposure, and that they are therefore confounders which could give rise to spurious associations between ETS and lung cancer. Few of the studies of ETS and lung cancer have controlled for potential confounding factors.

4) Estimates based on the relative risk of lung cancer for nonsmokers married to smokers, such as the relative risk of 1.3 used in the Geomet report, are much higher than would be expected from comparisons of the biological markers of smoke exposure between ETS-exposed persons and active smokers. Such dosimetric comparisons, coupled with low-dose extrapolation from data on smokers, lead to risk estimates which are several hundred to several thousand times smaller than estimates based on the ETS epidemiologic data. For example, Robins *et al.* (1989) estimate that, based on dosimetric calculations of respirable suspended particulates, the cigarette equivalent of ETS exposure ranges from .0001 to .005 cigarettes per day (that is, 0.4 to 1.8 cigarettes per year). Extrapolating from a model fit to the British doctor cohort smoking data

(Moolgavkar *et al.*, 1989), those cigarette equivalents correspond to lung cancer relative risks of 1.00003 to 1.0015 for ETS exposure from age 22.5 to age 60. For exposure from birth to age 60, the extrapolated relative risks are 1.00015 to 1.0074. These estimates are miniscule in comparison with the summary relative risk of 1.3 derived from the epidemiologic data.

Such huge discrepancies cast doubt on the validity of the observed association between ETS and lung cancer and suggest that the epidemiologic results are more likely explained by bias and confounding than by an effect of ETS exposure.

Conclusion

Although the authors of the DOT report acknowledge that there are several other published methods for calculating cancer risk, they fail to tell the reader that other methods have produced risk estimates that are several hundred to several thousand times lower than the ones contained in this report. The risk assessment portion of this document is badly flawed and adds nothing of value to the debate about the safety of exposure to ETS.

The problems of weak exposure measures and the lack of control of misclassification and confounding in epidemiologic studies, as well as problems of inconsistency and uncertainty in ETS risk analysis approaches, should have been discussed in the DOT report. Consideration of these issues leads to the conclusion that the basic requirements of a valid cancer risk assessment are missing. Better ETS epidemiology is needed to fill crucial data gaps with respect to causation and dose-response. Until such data are available, the smoking epidemiology coupled with dosimetric observations does not support the assertion that exposure to ETS causes lung cancer in flight attendants and crews, in passengers, or in anyone else.

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Because public trust and sound health policy are undermined by poor science, we urge Congress to hold all parties to the ETS debate to a higher standard of scientific evidence and reasoning than is displayed in the DOT report.