Appendix 3:
CONCAWE comments to the HRAPIE project

Concentration Response Functions for Morbidity Endpoints under the Project HRAPIE

A review of the concentration response functions for morbidity endpoints under the HRAPIE project was conducted. The purpose of this review was to provide a critique on the use of concentration response functions (CRFs), endpoints and its scientific relevance for use in the CBA. In addition, the current CBA analysis was compared to the scientific data used in the previous EU CAFE programme in the 2004 timeframe.

Endpoint: Bronchitis

The entire impact of the contribution of particulate matter on the incidence of bronchitis is inappropriately attributed to the fine particle fraction. This defies well-known biological facts concerning the etiology of bronchitis and highlights the need for clinical input into the CAFE CBA. It is very well known that bronchitis is primarily a disease of the upper respiratory tract. Therefore, coarse particles, which deposit in the upper respiratory tract, are much more likely to contribute to the etiology of this disease. Fine particles, which deposit in the lower respiratory tract, are not expected to contribute to the incidence of bronchitis. Therefore, it is not biologically appropriate to convert the morbidity function from a study using PM_{10} to $PM_{2.5}$. Rather, for bronchitis, a separate benefits analysis for PM_{10} or other coarse particle metric such as $PM_{2.5-10}$ or TSP should be provided. It is critical to note that in the study by Abbey et al, a stronger relationship was observed for TSP, the actual metric of particle exposure used, than for PM_{10} or $PM_{2.5}$. Therefore, valuation of bronchitis attributed to $PM_{2.5}$ should not be performed under the CAFE programe.

An appropriate method to convert the exposure response function (ERF) based on PM_{10} to an ERF based on $PM_{2.5}$ was not used in the CBA. The authors of the CBA take the attack rate for chronic bronchitis based on PM_{10} and adjust to get the results for $PM_{2.5}$. In our view, the attack rate should be adjusted to get the $PM_{2.5}$ fraction, and then taken out $PM_{2.5}$. Assume that 54% of the PM_{10} attack rate is due to $PM_{2.5}$. (A conversion factor of 1.54 is used). As such, 54% of the attack rate based on PM_{10} (which is 7%) becomes a 3.8% attack rate (54% x the 7%) PM_{10} attack rate = 3.8%). So, if 54% of the PM_{10} exposure is $PM_{2.5}$, this means a 10 ug/m^3 PM_{10} ERF is 5.4% $PM_{2.5}$. Final adjustment should be 5.4 ug/m^3 / 3.8% attack rate = 0.7% adjusted attack rate for $PM_{2.5}$. This compares with the authors adjusted rate of 1.07%.

The ERFs used were not for the air pollutant under consideration. Since monitoring of both PM_{10} and $PM_{2.5}$ was very limited in California before 1986, Abbey et al. used data for TSP to derive estimates for PM_{10} and airport visibility records to derive estimates for $PM_{2.5}$. This unwieldy approach to exposure estimate seriously jeopardized the findings from the study.

The assessment of bronchitis is based on a single study (ASHMOG Abbey et al., 1995a) for which the result was not even statistically significant at the 5% level. Causality cannot be established based on the results of a single ecological epidemiology study. Further, the accuracy of an ERF based on a single study result needs scientific justification, and in particular, the accuracy of the adjustment for smoking in this study, the major contributor to the incidence of bronchitis. The authors make the assumption that no smoking occurred in the cohort of seventh day Adventists. The higher lung cancer rates for males versus females in this study raises concern for this assumption. Further, 15% of the subjects in the study had smoked prior to 1977 and were then assumed to stop smoking when they became seventh day Adventists. Thirty percent of the study subjects lived with a smoker, and 42% had worked with a smoker. Further, the shear size of the risk due to PM air pollution, which is essentially the same size as the background rate attributed to all other factors, raises more suspicion. Finally, it is questionable to use an ERF based on a result that was not statistically significant at the 5% level. This brings into the question the concept of whether the findings from a single study are robust enough to conclude in the *primary or core* portion of a CBA. It is unlikely that such an approach would be normally justified and the CAFE CBA should apply a scientific process to accommodate and accept recommendations of the reviewers.

Using data from California during the period of 1966-1988 when air pollution was high, likely resulting in an inflated ERF. The authors of the CBA chose to partially justify inclusion of this endpoint based on reference to "modern" HIAs. The air pollution data that are the basis of the study used for the CBA are from 1966-1987, or close to 30 years old. It is questionable whether ERFs based on results from another continent using air pollution data from 30 years ago are sufficiently robust to use in a CBA designed to project results nearly 20 years into the future, a near 60 year extrapolation.

Using an ERF derived from high air pollution levels relevant to current, and with a different air pollution mix relative to those in Europe today requires further justification. Indeed, the air pollution data in California are dominated by photochemical smog. Likely, this ERF drastically over-estimates effects of low levels of PM alone. In fact, whether or not a threshold exists for this endpoint, and whether or not the ERF is specific to particulate matter, photochemical pollution, other gases present in ambient air, or a combination of these, has not been evaluated.

A baseline disease rate from a single U.S.-based study and extrapolation to Europe is used without any adjustment or consideration of the uncertainties. Only limited information is provided on how baseline rates in the U.S. compare with those in the U.S. It is well know that smoking is by far the major contributor to the production of bronchitis. One might guess therefore that the incidence of this disease might differ in the Europe versus the U.S. according to difference in smoking rates. Nonetheless, the accuracy of basing a benefits analysis for bronchitis based on baseline disease rates from the U.S is questionable.

Restricted Activity Days (RADS) and Minor Restricted Activity Days (MRADS)

Assessment of these endpoints are based on the results of a single study, the Health Interview Study, as reported by Ostro et al., 1987, and Ostro and Rothschild, 1989. The ERFs are derived from a study from another continent and during the period of 1976-1981, or close to 30 years ago, when the air pollution levels were higher. The validity of extrapolating from results in 1976 to 2020 and beyond, or close to a 50 year extrapolation is questioned. In the case of particulate matter, the tenuous exposure metrics used in this study is questioned and requires justification. PM_{10} and $PM_{2.5}$ levels were not measured as part of this study. Rather, $PM_{2.5}$ levels were estimated from visibility data from airports. Results of other CBA assessments have indicated concerns for extrapolating results from high pollution levels to lower levels and resulting inflation of the ERF at higher levels. Further, there has been no assessment of whether RADs or MRADs would even be triggered by lower air pollution levels. In other words, the issue of threshold has not been explored at all for these morbidity endpoints.

In the case of particulate matter, the adjustment of an ERF for PM_{10} to one based on $PM_{2.5}$ based on the simple mean ratio of these particles in urban air, and this practice is inappropriate. The authors offer no biological explanation as to why such an adjustment is appropriate, or why fine PM would be expected to exhibit the same potency as coarse particles. Fine and coarse particles distribute differentially in the respiratory tract and as stated by the WHO and others, produce a different and separate spectrum of health effects. As described above, certain respiratory symptoms would be expected to be exacerbated more by exposure to coarse rather than fine PM, a finding consistent with the actual study results reported by Abbey et al., where stronger associations were observed for TSP than for PM_{10} or $PM_{2.5}$ surrogates. It is not clear why the authors of the CBA choose to attribute all RAD related effects to fine PM.

In the case of ozone, the plausibility of the association with MRAD, the ERF selected and how it is applied in the CAFE CBA is questioned. Ozone is a respiratory toxicant. In the study by Abbey et al., no association was reported between exposure to ozone and *respiratory* restricted activity days (RRADs). This raises the question, if those in the study were not restricted due to respiratory-related reasons, what biologically related reason accounts for their restricted activity that could be due to ozone exposure? Using a multi-pollutant model applied to air pollution data between 1976 and 1981, the author's report a positive association between a 2-week average 1-hour ozone concentrations and MRAD. However, temperature is incorporated linearly in their mode and is highly correlated with ozone, which decreases the certainty that ozone alone is causing MRADs. In addition, there was high variance in the regression coefficients across the six years examined, with negative coefficients observed in 1977 and 1981 and a non-significant coefficient reported in 1976. Therefore, the conversion used by the authors of the CBA to convert an ERF based on 1-hr maximum levels to daily 8-hr averages should be properly justified. There is absolutely no question that higher peak concentrations of ozone produce more pulmonary effects than lower average levels. It is entirely possible that at lower average ozone levels, no respiratory effects and no MRADs would occur. However, the authors of the CBA did not consider this possibility and instead make the conversion to 8-hour average values, and extrapolate down to 35 ppb ozone, a level producing no clinical effects.

All effects of air pollution on RADs and MRADs are being arbitrarily attributed to fine PM and ozone, with potential effects of other pollutants ignored. For example, we note that in a multi-pollutant model, the hypothesized effect of exposure to $PM_{2.5}$ on RAD did not persist following adjustment for carbon monoxide (Steib et al, 2002).

The health endpoints of RAD and MRAD are highly subject to socioeconomic confounding. In the study used to derive the ERFs, significant city to city differences in RAD rates were observed. This was likely due to socioeconomic factors and other factors that were not adequately controlled in the selected study. Some of these factors include time spent

outdoors, building construction, health practices including how such days are recorded, age of the population, sex, race, education, income, marital status, temperature, employment conditions and rates, smoking rates, and many other factors. Even greater differences would be expected when considering cities in the U.S. versus those in Europe. Further, many of the socioeconomic factors that need to be controlled to identify the potential effect of air pollution are likely much more important than air pollution itself in the production of RADs and MRADS. The analogy is attempting for a single drop of water inside an ocean, or a single ant within a colony of ants.

The RAD background rate taken from a U.S.-based study (ORNL/RFF, 1994) and inappropriately applied it to Europe's CBA. Socioeconomic factor such as disability rates, income status, unemployment rates, and various definitions of RAD will influence the background rates, and these factors were not considered.

In summary, all of the above indicate significant concerns for the transferability of these EFRs for use in assessing RAD and MRAD in "average Europe", without any consideration for all of the uncertainties involved. Certainly, such "benefits" should not be included in the core CAFE CBA assessment, either for particulate matter or for ozone. In the case of particulate matter, any estimates that are made should be attributed to coarse PM rather than fine PM.

References

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