

**ALTERNATIVE APPROACHES FOR ESTIMATING  
HEALTH-RELATED QUALITY OF LIFE IMPACTS:  
NONROAD ENGINE AIR EMISSIONS REGULATION CASE STUDY**

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## PREFACE

This case study was one of three developed to support the work of the Institute of Medicine's Committee to Evaluate Measures of Health Benefits for Environmental, Health, and Safety Regulation. The Committee's summary of this case study, as well as the results of its other investigations and deliberations, is provided in its final report, *Valuing Health in Regulatory Cost-Effectiveness Analysis (2006)*.

This more detailed version of the case study contains additional information that may be of interest to regulatory analysts and other researchers. However, it was largely completed prior to the articulation of the Committee's conclusions and recommendations and thus does not reflect all of the views presented in the Committee's final report.

The case studies were undertaken as a learning experience, to provide the Committee with information on the challenges associated with applying different health-related effectiveness measures in a regulatory context. Due to time and budget limitations, they do not replicate the full complexity and level of detail required for regulatory analysis under current government-wide guidance or under the Committee's final recommendations. The case studies relied extensively on the voluntary efforts of many individuals.

## ACKNOWLEDGEMENTS

This case study could not have been completed without the hard work and dedication of a number of volunteers. The Committee is grateful for the extensive efforts of those who assisted in its completion, which contributed enormously to the Committee's understanding of the challenges and opportunities associated with conducting cost-effectiveness analysis in a regulatory context.

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## SECTION 1.0: INTRODUCTION

The Institute of Medicine's (IOM's) Committee to Evaluate Measures of Health Benefits for Environmental, Health, and Safety Regulation commissioned three case studies as part of its investigations related to the use of cost-effectiveness analysis to assess the impacts of economically significant federal health and safety regulations. These case studies allowed the Committee to explore the application of alternative approaches to estimating health-related quality of life (HRQL) impacts in the regulatory context, and were one of many inputs into its deliberations.

This report provides a detailed account of the Committee's third case study, which addresses an U.S. Environmental Protection Agency (EPA) regulation establishing standards for air pollution emissions from nonroad engines. We selected this regulation because it allowed us to explore issues related to valuing the effects of chronic illness and preventable mortality. In addition, EPA air pollution rules account for a sizable fraction of the rules likely to be affected by the Committee's recommendations, and provide examples of rules with quantified non-health (e.g., ecological) benefits as well as potentially significant health and non-health benefits that cannot be quantified.

In this case study, we apply different HRQL approaches to three health conditions associated with exposure to fine particulate matter (PM<sub>2.5</sub>): preventable mortality, chronic bronchitis, and nonfatal acute myocardial infarction (AMI). We focus on these endpoints because they account for the majority of the benefits of EPA's nonroad regulations; however, the rule will also reduce the incidence of a number of other health effects as well as provide non-health benefits (such as improved visibility).

To assess the HRQL impacts of chronic bronchitis and nonfatal AMIs, we used three different approaches (the Committee's report provides information on its recommendations for future conduct of these types of analyses):

1. We asked clinical experts to locate the disease descriptions for each condition according to the attribute levels used in the EuroQol EQ-5D index, then used the standard U.S. preference weights for this index to determine the value of each health effect.<sup>1</sup> This weighting process arrays the values on a scale anchored at zero and one, where zero corresponds to death and one corresponds to perfect health, based on community preferences.
2. We used preliminary estimates from a recently published catalogue of EQ-5D weights for chronic conditions to determine the HRQL decrement associated with each condition. This catalogue is based on data from the Medical Expenditure Panel Survey (MEPS) and was developed by Patrick Sullivan, William Lawrence, and Vahram Ghushchyan.

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<sup>1</sup> We used clinical experts rather than patients to complete this exercise due to the limited time and resources available for this analysis.

3. We selected estimates from studies in the Harvard Cost Effectiveness Analysis (CEA) Registry, based on research completed by Carmen Brauer and Peter Neumann. The selection criteria addressed the extent to which (a) the health condition assessed in the study matched the health condition addressed by the regulation, and (b) the study complied with “best practices” for this type of valuation, based largely on the recommendations of the Panel on Cost-Effectiveness in Health and Medicine (Gold et al, 1996).

Under all three approaches, we used the same EQ-5D estimates to value preventable mortality, comparing a HRQL of “zero” to the age-specific HRQL that would be otherwise expected over the remainder of an average U.S. life span. Throughout the analysis, we compare “with condition” HRQL to average HRQL for the U.S. population of the same age, derived in most cases from MEPS data.

In the case study, we focus on annual impacts for simplicity and comparability, assessing the change in disease incidence attributable to a single year of the regulatory intervention. The new cases prevented each year will have longer term impacts, however, if the health effect is chronic or long-lived. In addition, for some health effects there may be a lag between the exposure reduction and the reduction in incidence. We take these future year impacts into account, using discounting to reflect the timing of the impacts. Agency regulatory analyses generally take a longer term view, and assess the impacts of the rulemaking over a multi-year period as well as on an annual basis.

This case study was developed as a learning experience for the Committee, and provided an opportunity to use the information available to regulatory analysts to develop different effectiveness measures. Due to time and budget limitations, it does not replicate the full complexity of EPA’s regulatory analysis. It involves the use of simplified analytic approaches and assumptions that rely largely on mean or median estimates, and provides limited information on the range of possible values and the distribution of impacts across population subgroups. In these and other respects, the case study does not fully adhere to the existing guidelines for regulatory analysis nor to the recommendations developed by the IOM Committee. The lessons learned from this case study are discussed in the Committee’s report.

The following sections describe our analytic approach and findings in detail; a summary of this case study is available in Appendix A of the Committee’s final report. First, we summarize the original EPA regulatory analysis. Next, we discuss our analytic approach. The following section presents our results, and the last section then discusses the limitations of our analysis. The appendices provide supplementary information on selected topics.

## SECTION 2.0: EPA ANALYSIS

EPA's nonroad diesel rule was the third in a series of similar rules designed to reduce harmful air emissions from mobile sources. It both set emissions standards for new engines and limited the amount of sulfur allowed in diesel fuel. The emissions standards address engines used in most construction, agriculture, industrial, mining, and airport equipment -- such as loaders, dozers, backhoes, tractors, and off-road trucks. The sulfur standards address fuel used in locomotives and marine vessels as well as in the types of nonroad diesel engines listed above. In addition to reducing harmful emissions directly, the sulfur standards for fuel were designed to allow engine manufacturers to use less polluting technology.

These requirements limit direct emissions of fine PM as well as other pollutants that form PM once emitted and/or that contribute to the creation of ozone. The pollutants addressed include nitrogen oxides (NO<sub>x</sub>), sulfur oxides (SO<sub>x</sub>), nonmethane hydrocarbons (NMHC), carbon monoxide (CO), and toxic volatile organic compounds (VOCs).

The engine emissions standards were authorized primarily under Section 213 of the Clean Air Act, which requires that EPA address NO<sub>x</sub> and other pollutants that may harm human health and welfare. This section instructs EPA to set standards that achieve the largest emissions reduction achievable through the use of available technology, and allows the EPA Administrator to consider the cost, lead time, noise, energy, and safety factors associated with the application of such technology when establishing the standards. The fuel standards are authorized primarily by Section 211(c) of the Act, which requires EPA to regulate fuels as needed to reduce adverse effects on human health or welfare as well as to prevent impairment of emissions control devices.

The proposed rule was published in the *Federal Register* in May 2003 and the final rule was published on June 29, 2004. The final engine and fuel standards will be phased-in between 2007 and 2015; EPA expects that, with replacement of older engines, almost all engines in use will meet the new requirements by 2030.

In developing this rule, EPA considered a number of regulatory options. In its draft regulatory analysis (completed in 2003), EPA assessed 12 options that differed in terms of the implementation schedule, the stringency of the standards, and the types of engines addressed. In the final (2004) regulatory analysis, EPA presented analytic results only for the final rule, reporting costs and benefits separately for the fuel component and for both the fuel and engine components combined. The final rule builds on one of the 12 options that was originally assessed, incorporating changes resulting from EPA's review of the public comments received as well as further research and analysis.

EPA's final assessment is briefly summarized below, based on information on the *Federal Register* notice and regulatory impact analysis (EPA 2004a, 2004b). Over the past several years, EPA's analytic approach has been reviewed by a number of independent expert panels convened under the auspices of EPA's Science Advisory Board and the National

Academies' National Research Council, and it continues to evolve as more research and analytic tools become available.

## 2.1 Cost Analysis

For the nonroad rule, EPA's cost analysis addressed the impacts of the rule at several levels of aggregation. EPA calculated the short and long term impact of the rule on the costs of producing and operating individual engines of various types as well as on the costs per gallon of refining and distributing fuel. EPA aggregated these costs, then used a multi-market economic impact model to assess the effects of these cost changes on the prices and quantities of commodities traded. In addition, EPA considered social welfare impacts, including the ultimate distribution of the costs across various groups of producers and consumers. EPA also estimated the impact of the rule on small engine and equipment manufacturers, as well as on small fuel refiners and distributors, as required under the Regulatory Flexibility Act as amended by the Small Business Regulatory Enforcement Fairness Act.

The results of these analyses indicated that the social welfare costs of the final rule would total approximately \$2.0 billion annually as of 2030, when virtually all engines in use are expected to meet the standards.<sup>2</sup> EPA also reports the present value of the costs incurred over 30 years of rule implementation. The present value (in 2004) of the costs incurred from 2007 (when the requirements begin to take effect) through 2036 is estimated as \$27 billion using a three percent discount rate, or \$14 billion using a seven percent discount rate.<sup>3</sup> EPA expects that the rule may ultimately lead to about a 0.1 percent increase in the prices of goods and services affected by these costs. The cost estimates were accompanied by several analyses of uncertainty, including assessment of the sensitivity of the estimates to changes in the values of key parameters. EPA noted that the uncertainty in its cost estimates may be in the range of about  $\pm 20$  percent, leading to an uncertainty range of approximately \$1.7 billion to \$2.6 billion for the year 2030.

EPA also reported the costs per ton of emissions reduced under several different scenarios, allocating the costs of the rule across the major types of pollutants addressed. For example, as of 2030, EPA estimated that the rule would cost approximately \$680 per ton of NO<sub>x</sub> and NMHC emissions reduced, \$9,300 per ton for PM, and \$810 per ton for SO<sub>x</sub>.<sup>4</sup> The other cost-per-ton scenarios that EPA presented include considering only the fuel component of the regulations, calculating present values using different discount rates, and presenting sensitivity analyses that use alternative estimates of the size of the nonroad fleet (and its fuel consumption) and of the amount of engine emissions.

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<sup>2</sup> All estimates are presented in 2000 dollars unless otherwise noted.

<sup>3</sup> The use of these two discount rates is consistent with current Office of Management and Budget (OMB) guidance (OMB 2003). The rates reflect differing assumptions regarding the opportunity costs of regulations; i.e., whether they are more likely to affect investment or consumption.

<sup>4</sup> Reported as 2002 dollars.

## 2.2 Risk Assessment

To determine the impact of the modeled emissions changes on human health, EPA relied on recent recommendations from two expert panels (convened under the auspices of the National Research Council and EPA's Science Advisory Board), as well as its own review of the literature. EPA used data from selected epidemiological studies to estimate the effects of emissions reductions on mortality for adults and infants, and on different types of respiratory and cardiovascular morbidity (EPA 2004a, Chapters 2 and 9). These studies were translated into health impact algorithms that use concentration-response functions to predict the change in incidence attributable to changes in pollutant levels, based on estimates of baseline incidence and the characteristics of the affected population.

For this and many of its other recent air regulations, EPA used its BenMAP model to predict changes in the incidence of health effects (and resulting benefits values).<sup>5</sup> BenMAP accepts output from EPA's air quality models, which estimate the changes in pollution levels associated with different regulatory options. BenMAP provides mean estimates of benefits as well as information on the distribution of impacts. The model is based on detailed Census data and various forecasting models, and allows reporting by age, sex, and race as well as geographic location. To determine the baseline incidence of each health effect in the absence of the regulations, EPA uses different data sources selected to match the epidemiological studies for each health endpoint. For example, for the nonroad rule, baseline (without the regulation) mortality was estimated from data from the Centers for Disease Control and Prevention (CDC) that are broken out by county and age. The baseline incidence estimates for the other (nonfatal) respiratory and cardiovascular effects were derived from various national data sets and related studies.

EPA considered a number of criteria in selecting the epidemiological studies and effect estimates used in this model for the nonroad rule. EPA notes that "[i]n general, we selected effect estimates that 1) most closely match the pollutants of interest, i.e. PM<sub>2.5</sub>, 2) cover the broadest potentially exposed population (i.e. all ages functions would be preferred to adults 27 to 35), 3) have appropriate model specification (e.g. control for confounding pollutants), 4) have been peer-reviewed, and 5) are biologically plausible" (EPA 2004a, p. 9-20). EPA also considered the need to avoid double-counting of health impacts as well as other factors that may affect the quality of the resulting analysis.

For preventable mortality among adults, EPA used a prospective long-term cohort study sponsored by the American Cancer Society because it was the most comprehensive study available with the longest follow-up period (Pope et al., 2002). For new cases of chronic bronchitis and nonfatal acute myocardial infarction, EPA selected studies by Abbey et al. (1995) and Peters et al. (2001) because they were the only U.S. studies which provided estimates of the link between PM<sub>2.5</sub> and these specific endpoints. The relative risk factors from these studies are reported in Exhibit 1 below; these factors represent the average increase in the risk of incurring the health condition associated with an increase in PM levels. Additional information on these

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<sup>5</sup> BenMAP is available at <http://www.epa.gov/ttn/ecas/benmodels.html>.

studies is provided in Section 3.1.1; more detailed information on the basis for these estimates, on the associated confidence intervals, and on their application in EPA's models, is provided in the source documents.

<b>Exhibit 1</b>	
<b>RELATIVE RISK FACTORS FOR KEY ENDPOINTS</b>	
<b>Health Endpoint</b>	<b>Risk Factor (average, 95 percent confidence interval)</b>
Chronic bronchitis	1.17 (1.02, 1.33)
Nonfatal acute myocardial infarction	1.27 (1.06, 1.53)
Preventable mortality	1.06 (1.02, 1.11)
<p>Sources:            Chronic bronchitis: Abbey et al. (1995), p. 139.            Nonfatal acute myocardial infarction; Peters et al. (2001)            Preventable mortality: Pope et al. (2002), p. 1136, Table 2.            Email from Bryan Hubbell to Lisa Robinson, June 1, 2005.</p> <p>Notes:            Excludes acute and short-term endpoints included in EPA analysis            Chronic bronchitis estimates exclude reversals which are subtracted from the resulting risk estimates; these reversals affect 47 percent of the incident cases.            See source documents and EPA (2004a, 2004b) for more detailed information on uncertainty and on the application of these factors in EPA's assessment.</p>	

A variety of additional studies were used for the other respiratory and cardiovascular endpoints assessed. EPA explored the uncertainties in these estimates both qualitatively and quantitatively, and provided separate estimates of impacts on certain subgroups of concern, such as asthmatic children.

### **2.3 Benefit Valuation**

EPA's benefits analysis provides quantified estimates for only some of the expected impacts of the rule on human health and the environment, due to limitations in the available research and data. EPA was able to quantify the effects of PM exposure on mortality and on a variety of select respiratory and cardiovascular effects, as well as its impact on visibility at a subset of potentially affected recreational areas.<sup>6</sup> EPA generally was not able to quantify the benefits of reducing ozone or pollutants other than PM due to limitations in air quality modeling, although the results of preliminary modeling of ozone impacts are reported in its regulatory impact analysis.

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<sup>6</sup> This analysis includes both the direct effects of PM and sulfate emissions as well as the contributions of SO<sub>2</sub> and NO<sub>x</sub> to PM.

To quantify the PM-related benefits, EPA first considered the impacts of the rule on air quality, and then estimated the effects of changes in air quality on selected health endpoints as well as on visibility. Developing and operating the sophisticated emissions and air quality models needed to assess these kinds of impacts is very expensive and time-consuming, and EPA faced significant budget and schedule constraints in preparing the nonroad analysis. Hence EPA had to choose a set of PM standards to model early in the regulatory development process, and then to scale and transfer the results to estimate the impacts of the final rule.<sup>7</sup>

To estimate the dollar value of these health impacts, EPA relied on approaches originally developed in the early 1990s to support retrospective study of the Clean Air Act and since modified based on several rounds of peer review and public scrutiny. To value preventable mortality, EPA applied a range of estimates of the value of statistical life (VSL).<sup>8</sup> Historically, EPA relied on a distribution of 26 values that resulted from a review of the VSL literature completed in the early 1990s. However, for the nonroad rule, EPA instead relied on two more recently completed meta-analyses that combine the results of numerous wage-risk studies (Mrozek and Taylor 2000, Viscusi and Aldy 2003).<sup>9</sup> Based on these studies, EPA assumed that the values are normally distributed with a mean VSL of \$5.5 million and a 95 percent confidence interval between \$1 million and \$10 million. EPA adjusted these estimates to reflect two factors: (1) the relationship between income growth over time and willingness to pay (WTP), and (2) the lag between exposure reduction and reduction in mortality rates.<sup>10</sup>

For chronic bronchitis and restricted activity days, EPA adapted dollar values from stated preference studies of individual WTP.<sup>11</sup> For other non-fatal respiratory and cardiovascular effects, EPA relied on data on the medical costs of illness (COI) and lost earnings due to the lack of suitable WTP estimates, recognizing that such COI estimates are an imperfect proxy for WTP and are likely to understate WTP under most scenarios. EPA also estimated changes in visibility at 86 recreational areas (a subset of all areas at which EPA expected visibility would be

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<sup>7</sup> Such scaling was not possible for ozone because of the non-linear nature of the relationships.

<sup>8</sup> VSL refers to the value of small changes in mortality risk spread throughout a large population; e.g., an 1 in 10,000 change in an individual's risk of preventable mortality. It is not the value of saving the life of an identifiable individual; rather, it is the amount that individuals are willing and able to pay for risk reductions that sum to one statistical life. EPA is currently reviewing and refining its approach for estimating VSL.

<sup>9</sup> Wage-risk studies are a revealed preference method that uses labor market data to establish the relationship between wages and the risk of on-the-job fatalities across a broad spectrum of industries. Researchers use statistical methods to separate out the effects of other factors on wages, so that the results indicate only the incremental wage differential needed to compensate workers for added risk.

<sup>10</sup> To adjust for changes in real income over time (i.e., changes in average gross domestic product per capita), EPA relied on estimates of the relationship between income and WTP determined separately for minor health impacts, severe or chronic health impacts, and preventable mortality. (Generally, WTP is expected to increase as income increases, but not necessarily by the same proportion.) To adjust for the lag between pollution reductions and reductions in mortality, EPA assumed that 25 percent of the averted cases would occur in the first year, 25 percent in the second year, and 16.7 percent in each of the three following years. EPA has since modified its approaches for making these adjustments (see EPA 2005).

<sup>11</sup> Stated preference methods use contingent valuation surveys or other approaches that allow researchers to ask respondents what they would be willing to pay for a specified risk reduction.

affected), and estimated the dollar value of the resulting benefits based on a contingent valuation survey of WTP for visibility improvements at these areas.

The results of these analyses allowed EPA to quantify the following annual PM-related impacts as of the year 2030, when virtually all engines in use are expected to meet the standards. As indicated by Exhibit 2, EPA’s primary estimates of monetized benefits total \$80 billion (using a seven percent discount rate) to \$83 billion (using a three percent discount rate) in that year.<sup>12</sup> The dollar value of these benefits is determined largely by the impact of averted mortality, which represents over 90 percent of the monetized effects.

<b>Exhibit 2</b>		
<b>QUANTIFIED AND MONETIZED BENEFITS OF EPA’S NONROAD DIESEL RULE (primary estimate for the year 2030, millions of 2000 dollars)<sup>a</sup></b>		
<b>Endpoint</b>	<b>Avoided Incidence (cases/year)</b>	<b>Monetary Value (in millions)</b>
Preventable mortality: Long-term exposure (adults, 30 and over) <sup>b</sup>	12,000	\$72,000 - \$77,000 <sup>e</sup>
	22	\$150
Infant mortality (infants, under one year)	5,600	\$2,400
Chronic bronchitis (adults, 26 and over)	15,000	\$1,200
Non-fatal myocardial infarctions (adults, 18 and older)	5,100	\$92
Hospital admissions—Respiratory (adults, 20 and older) <sup>d</sup>	3,800	\$83
Hospital admissions—Cardiovascular (adults, 20 and older) <sup>e</sup>	6,000	\$1.7
Emergency room visits for asthma (18 and younger)	13,000	\$5.2
Acute bronchitis (children, 8–12)	200,000	\$9.2
Asthma exacerbations (asthmatic children, 6–18)	160,000	\$2.7
Lower respiratory symptoms (children, 7–14)	120,000	\$3.2
Upper respiratory symptoms (asthmatic children, 9–11)	1,000,000	\$130
Work loss days (adults, 18–65)	5,900,000	\$320
Minor restricted activity days (adults, 18–65)	N/A	\$1,700
Recreational visibility impairment (86 areas)	N/A	\$80,000 - \$83,000
<b>Monetized Total<sup>f</sup></b>	N/A	\$80,000 - \$83,000

Source: EPA (2004b), pp. 39134-39135, Tables VI.E-1 and VI.E-2.

Notes:

- EPA reports estimates rounded to two significant digits; detail does not add to total due to rounding.
- EPA assumes that preventable mortality associated with ozone is captured in this estimate.
- Range reflects use of 3 or 7 percent discount rate.
- Respiratory hospital admissions for PM include admissions for chronic obstructive pulmonary disease, pneumonia, and asthma.
- Cardiovascular hospital admissions for PM include total cardiovascular admissions and admissions subcategories for ischemic heart disease, dysrhythmias, and heart failure, excluding myocardial infarction to avoid double-counting.
- Total excludes nonmonetized health and welfare benefits and does not reflect EPA’s analyses of uncertainty.

<sup>12</sup> Although the estimates presented in the exhibit are for a single year, discounting is used to adjust certain of the monetary values to better reflect the timing of the impacts (e.g., the lag between exposure reduction and reduction in incidence).

In addition to the primary benefits estimates reported in Exhibit 2 above, EPA used a number of different approaches to provide information on the uncertainty in these estimates. The supporting documents provide relatively extensive qualitative discussions of uncertainty as well as several types of quantitative analysis. EPA ultimately concluded that it is not possible to quantify the uncertainty in its emissions estimates due to the numerous factors involved, and focused its attention largely on the concentration-response functions used in its assessment of health impacts.

The final regulatory impact analysis includes the results of two experimental efforts to quantify selected uncertainties in the benefits assessment: (1) a Monte Carlo (probabilistic) statistical analysis based on the standard errors reported in the underlying studies, and (2) a pilot expert elicitation process focused on the estimates of PM-related mortality. In addition, EPA presented sensitivity analyses that explore alternative approaches for selected key assumptions. For example, for preventable mortality, EPA assessed the use of different concentration-response functions as well as alternative assumptions regarding the lag between reduced exposure and reduced incidence and the presence of threshold effects. EPA found that the use of alternative concentration-response functions alone can potentially double the estimates of averted cases of mortality.

The results of EPA's cost and benefit analyses indicated that the monetized net benefits (benefits minus costs) of the final rule will total approximately \$78 to \$81 billion annually as of 2030, depending on whether a seven or three percent discount rate is applied.<sup>13</sup> The present value (in 2004) of the net benefits incurred from 2007 (when the rule's provisions begin to take effect) through 2036 is estimated as \$340 billion using a seven percent discount rate, or \$780 billion using a three percent discount rate.

In addition to the uncertainty in the quantified effects discussed earlier, these results reflect uncertainty related to the magnitude of the many benefits that could not be quantified. EPA concluded that the monetized benefits may significantly understate the total benefits of the regulations because they exclude health, odor, and ecological benefits associated with reductions in CO, VOCs, air toxics, and ozone. Exhibit 3 provides EPA's summary of the nonquantified effects associated with each pollutant.

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<sup>13</sup> In the annual estimates, this range results because of the use of different discount rates to reflect the timing of the benefits. In particular, the cases averted by a year of rule implementation include some delayed effects; i.e., the lag between reduced exposure and reduced incidence for preventable mortality as well as the effects of reducing chronic illness over the affected individuals' life spans. In the estimates of multi-year impacts, discounting is also used to calculate the present value of the costs and benefits incurred in future years.

**Exhibit 3**

**NONMONETIZED BENEFITS OF EPA'S NONROAD DIESEL RULE**

<b>Pollutant</b>	<b>Nonquantified Effects</b>
Ozone Health	<p>Premature mortality<sup>a</sup>                      Respiratory hospital admissions.                      Minor restricted activity days.                      Increased airway responsiveness to stimuli.                      Inflammation in the lung.                      Chronic respiratory damage.                      Premature aging of the lungs.                      Acute inflammation and respiratory cell damage.                      Increased susceptibility to respiratory infection.                      Non-asthma respiratory emergency room visits.                      Increased school absence rates.</p>
Ozone Welfare	<p>Decreased yields for commercial forests.                      Decreased yields for fruits and vegetables.                      Decreased yields for non-commercial crops.                      Damage to urban ornamental plants.                      Impacts on recreational demand from damaged forest aesthetics.                      Damage to ecosystem functions.</p>
PM Health	<p>Low birth weight.                      Changes in pulmonary function.                      Chronic respiratory diseases other than chronic bronchitis.                      Morphological changes.                      Altered host defense mechanisms.                      Cancer.                      Non-asthma respiratory emergency room visits.</p>
PM Welfare	<p>Visibility in many Class I areas.                      Residential and recreational visibility in non-Class I areas.                      Soiling and materials damage.                      Damage to ecosystem functions.</p>
Nitrogen and Sulfate Deposition Welfare	<p>Impacts of acidic sulfate and nitrate deposition on commercial forests.                      Impacts of acidic deposition to commercial freshwater fishing.                      Impacts of acidic deposition to recreation in terrestrial ecosystems.                      Reduced existence values for currently healthy ecosystems.                      Impacts of nitrogen deposition on commercial fishing, agriculture, and forests.</p>
CO Health	<p>Premature mortality<sup>a</sup>                      Behavioral effects.</p>
HC Health	<p>Cancer (benzene, 1,3-butadiene, formaldehyde, acetaldehyde).                      Anemia (benzene).                      Disruption of production of blood components (benzene).                      Reduction in the number of blood platelets (benzene).                      Excessive bone marrow formation (benzene).                      Depression of lymphocyte counts (benzene).</p>

**Exhibit 3**

**NONMONETIZED BENEFITS OF EPA'S NONROAD DIESEL RULE**

HC Welfare	Reproductive and developmental effects (1,3-butadiene). Irritation of eyes and mucus membranes (formaldehyde). Respiratory irritation (formaldehyde). Asthma attacks in asthmatics (formaldehyde). Asthma-like symptoms in non-asthmatics (formaldehyde). Irritation of the eyes, skin, and respiratory tract (acetaldehyde). Upper respiratory tract irritation and congestion (acrolein).  Direct toxic effects to animals. Bioaccumulation in the food chain. Damage to ecosystem function. Odor.
<p>Source: EPA (2004B), p. 39139, Table VI.E-6.</p> <p>Notes:</p> <p>a. EPA assumed that the quantified impacts of PM on premature (preventable) mortality also capture any mortality benefits associated with other air pollutants.</p> <p>b. Many of the key hydrocarbons (HCs) addressed by this rule are also hazardous air pollutants listed in the Clean Air Act.</p>	

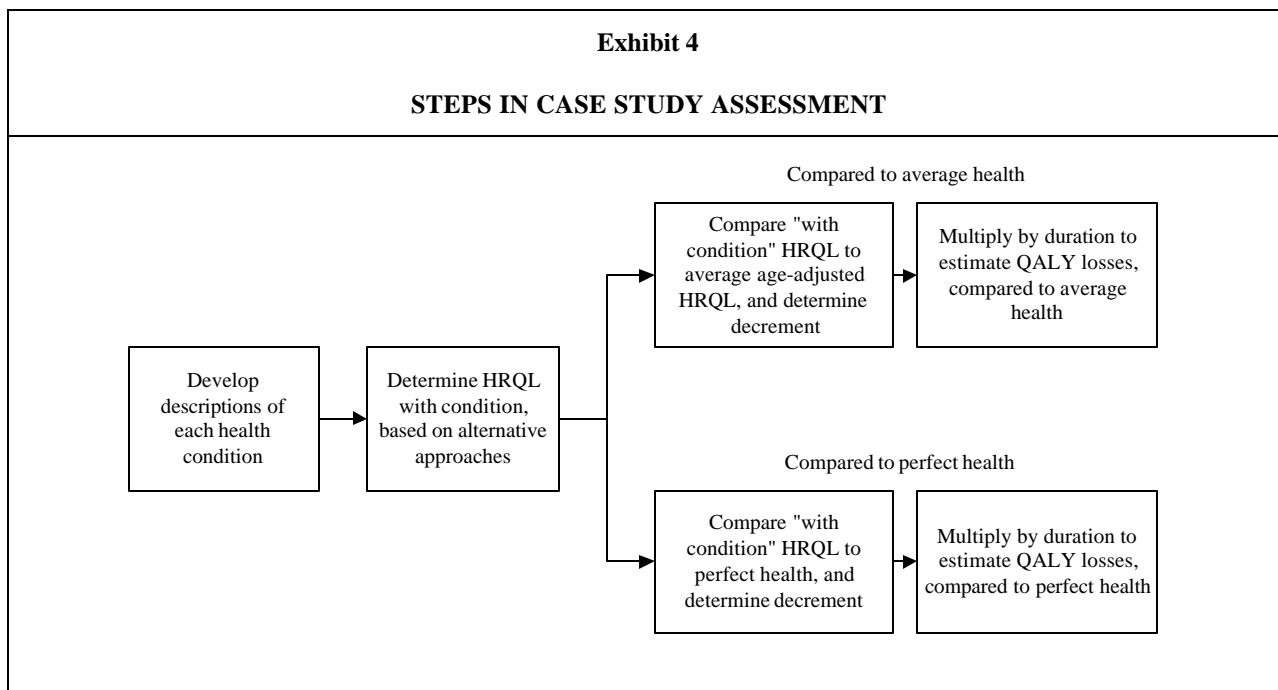
## **SECTION 3.0: CASE STUDY APPROACH**

For this case study, we applied three different approaches to assess the health-related quality of life (HRQL) and longevity impacts of EPA's nonroad rule, focusing on preventable mortality, nonfatal chronic bronchitis, and nonfatal acute myocardial infarction (AMI). Our first approach involved applying the EQ-5D using an expert judgment process. We asked medical experts to assign the attribute descriptions that best reflect the likely impacts of each health state, then valued these health states based on the EQ-5D U.S. community weights. Second, we used preliminary estimates of HRQL decrements for each health state from a recently completed catalogue of EQ-5D values for chronic conditions developed by Sullivan et al. (2005). Third, we transferred values from selected studies from the Harvard Center for Risk Analysis' Cost-Effectiveness Analysis (CEA) Registry, based on a review conducted by Brauer and Neumann (2005). The Committee's final report discusses the strengths and weaknesses of these approaches, and suggests improvements to the methods used in this case study.

In the following sections, we first describe those aspects of the analysis that are common across all three approaches. We then describe how we tailored our approach for each of the three HRQL measurement processes.

### **3.1 General Approach**

For all of the HRQL approaches, we followed a similar process. First, we developed descriptions of each health condition, based on the risk studies used in EPA's analysis. Second, we determined the HRQL impacts for each condition; the details of this step varied depending on which HRQL approach was used. Third, we estimated the difference in HRQL with and without the condition under two scenarios: one assuming that affected individuals would be in average health for their age in the absence of the condition, and the other assuming that the affected individuals would be in perfect or optimal health. We multiplied the resulting HRQL decrement by the expected duration of each condition, taking into account the life expectancy of the affected population. This process resulted in estimates of the quality-adjusted life year (QALY) losses due to each condition under each of the HRQL approaches, as illustrated in Exhibit 4 and discussed in more detail below.



### 3.1.1 Disease Descriptions

For this case study, we focused on three of the health endpoints included in EPA’s analysis of the nonroad rule: preventable mortality among adults and infants, chronic bronchitis among adults, and cardiac disease among adults subsequent to nonfatal AMI. We selected these endpoints because they account for the majority of the benefits of the regulations and because the other endpoints (listed in Exhibit 2) present a number of practical and conceptual challenges in an HRQL framework. The available epidemiological research generally defines these other endpoints as individual short-lived events (e.g., hospitalizations, emergency room visits, exacerbations) rather than as new cases of disease attributable to the pollution. Many of these events primarily affect individuals with underlying pre-existing conditions (such as asthma) and the extent to which the regulations would alleviate the underlying conditions is uncertain. Hence for childhood asthma and other respiratory and cardiovascular conditions among both children and adults, EPA only estimates the number of events averted by the regulations, not the changes in overall disease progression or incidence. While we were unable to evaluate these additional endpoints given the time and resource constraints affecting this case study, such evaluation may be desirable within the framework of a regulatory cost-effectiveness analysis.

In conducting our assessments, we relied on the information used in EPA’s final regulatory impact analysis for the nonroad rule to the extent possible (EPA 2004). The starting point for the analysis was the three studies EPA used in assessing the risks averted by the regulations: Pope et al. (2002) for mortality, Abbey et al. (1995) for chronic bronchitis, and Peters et al. (2001) for nonfatal AMI. As needed, we supplemented these data with information from other sources. Most of this additional information was taken from a cost-effectiveness analysis of a one microgram reduction in PM<sub>2.5</sub> prepared by Bryan Hubbell of EPA (Hubbell 2004). While the Hubbell analysis considered a different reduction in pollution levels than the

reduction attributable to the nonroad rule and used population data from a different year (2000 rather than 2030), it reflects the same underlying risk studies and the same general modeling approach (i.e., EPA's BenMAP model).<sup>14</sup>

Below, we discuss the data we used to describe each condition, including our assumptions related to age at incidence, duration, and life expectancy for both nonfatal and fatal cases. In these discussions, we refer to "affected individuals" for simplicity. In reality, EPA's regulations lead to risk reductions among a large population rather than preventing cases of illness among identifiable individuals (the relative risk factors are presented earlier in Exhibit 1). Analysts generally refer to these risk reductions as "statistical cases" since they represent the aggregation of risks across individuals. For example, a regulation that prevents an individual risk averaging 1 in 10,000 from affecting a population of 10,000 individuals would prevent one statistical case, because  $(1/10,000) * 10,000 = 1$ .

**Preventable mortality:** EPA relied on a study by Pope et al. (2002) to assess the mortality averted by the nonroad regulations. This study used data on 500,000 adults from the American Cancer Society's prospective study of mortality, and combined it with data from air pollution monitoring. The researchers considered PM as well as other air pollutants, and assessed the impact on mortality from all causes, from lung cancer, and from cardiopulmonary disease, employing statistical models to separate out the effects of other risk factors such as diet, smoking, and occupational exposures.

EPA used the resulting risk factors for all cause mortality associated with PM<sub>2.5</sub> in its analysis, estimating that the nonroad rule would avert 12,000 cases of mortality annually as of the year 2030.<sup>15</sup> As discussed in more detail below, we assume that the affected individuals would have lived a normal life span in the absence of the pollution exposures addressed by the rule, and assume that this life span would be the same as the average for the U.S. population of the same age.

**Chronic bronchitis:** EPA's estimates of the number of new cases of chronic bronchitis averted by the regulations were based on work by Abbey et al. (1995). This study followed a cohort of 3,914 California residents, focusing on a population that was largely nonsmoking (Seventh Day Adventists) to limit the extent to which the effects of smoking confounded the estimates of cases of illness associated with air pollution. The participants were asked to complete a standardized questionnaire on respiratory symptoms in 1977 and again in 1987, with an 87 percent response rate. The researchers then used computer algorithms to classify individuals in terms of whether they had chronic bronchitis (as well as asthma or emphysema). Definite cases of chronic bronchitis were defined as "symptoms of cough (cough type) and/or sputum production (sputum type) on most days, for at least 3 mo/y, for at least 2 y" (Abbey et al., p. 140). The researchers classified the cases by severity (including whether they involved cough only or cough and sputum production), and by whether they were new or persistent. The

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<sup>14</sup> More information on the Hubbell study, as well as a recent application of the approach to EPA's Clean Air Interstate Rule, is provided in Appendix A.

<sup>15</sup> In this discussion, we focus on the deaths among individuals age 30 and higher because they represent the majority of cases avoided, but we also include infant deaths in our analysis. (EPA estimated that the rule would avert 22 infant deaths in the year 2030, based on a separate risk study).

reversal rate (i.e., cases that had definite symptoms in 1977 but not in 1987) was also calculated. The research team then compared these estimates to estimates of the cumulative ambient concentrations of PM in the study locations, using statistical regression models to estimate the change in the health effects attributable to differences in pollution levels.

Based on the risk factors from this analysis, EPA estimated that the nonroad rule would avert 5,600 new cases of chronic bronchitis in adults annually as of the year 2030. In our calculations, we assumed that these cases of chronic bronchitis would last for the remainder of the affected individuals' life spans and did not attempt to model the likely worsening of symptoms over time.<sup>16</sup> We also assumed that the affected individuals would live a normal life span, using the approach to assessing life expectancy discussed later in this section.<sup>17</sup>

***Nonfatal AMI and subsequent progression of cardiac disease:*** For AMI, the development of disease descriptions was more complicated because the underlying risk study did not include information on post-AMI disease progression. Our starting point was the study EPA used in the nonroad rule analysis (Peters et al., 2001). This study was based on interviews of 772 myocardial infarction patients in Boston in 1995 and 1996. The researchers compared data on these patients to data on hourly concentrations of PM<sub>2.5</sub> and other pollutants, using statistical methods to estimate the extent to which AMIs may have been triggered by short-term exposures to increased pollution levels. EPA estimated that the nonroad rule would prevent 15,000 nonfatal AMIs annually as of 2030, based on the risk estimates in this study.

To assess the progression of cardiac disease associated with these pollution-induced nonfatal AMIs, we generally followed the approach utilized in Hubbell (2004) and EPA (2005). These analyses estimate the likelihood that AMI survivors would develop angina and/or congestive heart failure, adapting a coronary heart disease model created for the Victoria Burden of Disease study (Vos 1999) and supplementing it with American Heart Association data on angina. The EPA analyses assumed that survivors of nonfatal AMIs would experience congestive heart failure and angina according to the probabilities presented in Exhibit 5.

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<sup>16</sup> A preferable approach would be to develop a longitudinal disease model that identifies the different phases of illness, their duration, and probability of occurrence, and to ask the experts to identify the domain attributes for each phase. However, development of such a model is quite difficult and would require more time and resources than were available for this case study.

<sup>17</sup> This assumption is likely to overstate "with condition" life expectancy, which may be shortened by chronic bronchitis.

<b>Exhibit 5</b>	
<b>ALLOCATION OF POST-AMI HEALTH STATES</b>	
Congestive heart failure AND angina	10.2 percent
Congestive heart failure WITHOUT angina	9.8 percent
Angina WITHOUT congestive heart failure	40.8 percent
WITHOUT congestive heart failure OR angina	39.2 percent
Total	100.0 percent
Source: Hubbell (2004), pp. 16 to 19, and EPA (2005), pp. G-24 to G-32. Note: These subcategories were not used in the nonroad rule analysis, which only considers the occurrence of the nonfatal AMI itself and separately estimates hospitalizations for other cardiovascular conditions (see Exhibit 2 above).	

Again, we assumed that all cases would last for the remainder of the affected individuals' life span, consistent with Hubbell (2004) and EPA (2005), and did not attempt to model the likely worsening of symptoms over time. As discussed below, our calculations take into account the life-shortening effects of cardiac disease.

***Age, duration, and life expectancy:*** In its nonroad regulatory analysis, EPA uses its BenMAP model to assess the likely distribution of the impacts of the regulations by location, age, race, and gender (see Section 2.0 above). We considered using this model for our analysis, but, due to the limited time and resources available, instead followed a simpler approach. For each health state assessed, we assumed that the age at incidence would be the same as the average age from EPA's distributions for the year 2000 (rather than 2030), as reported in Hubbell (2004).<sup>18</sup>

For duration and life expectancy, our assumptions varied depending on the health condition assessed. For preventable mortality, a key question is whether the affected individuals would have had the same remaining life span as the general population in the absence of the pollution. This issue has been the subject of some debate because air pollution-induced mortality occurs largely among the elderly, many of whom suffer from cardiac disease and other health problems that may result from exposure to air pollutants as well as other causes. Consideration of these pre-existing conditions raises double-counting issues (because the effects of morbidity prior to mortality are counted separately in EPA's regulatory analysis) and also raises questions about whether the reduction in life expectancy associated with the conditions themselves should be attributed to the air pollutants or to other causes.

Based on review of the literature and guidance from an independent expert panel, EPA generally assumes that the distribution of underlying conditions is the same as in the overall

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<sup>18</sup> These distributions for the year 2000 reflect a population that tends to be skewed towards younger ages than the projections for the year 2030.

population for pollution-induced mortality.<sup>19</sup> In other words, EPA assumes that the individuals dying prematurely due to air pollution exposure represent the same distribution of underlying health conditions as is evident in the general population for the same age groups. We follow this approach in our case study, and assume that life expectancy would be the same as the U.S. population average in the absence of the pollution-related mortality.

EPA also adjusts for the time lag between pollution reductions and reductions in mortality. For the nonroad analysis, EPA assumed that 25 percent of the averted cases of mortality would occur in the same year as the pollution reduction, 25 percent in the second year, and 16.7 percent in each of the three following years (EPA 2004, p. 9-23).<sup>20</sup> EPA has since refined its approach for making these adjustments; however, we use this five year lag structure in our analysis for consistency with EPA's assessment of the nonroad rule. We assume that 25 percent of the cases of preventable mortality would occur in the same year as the pollution reduction (2030), and the remainder would be distributed over the subsequent four years consistent with EPA's assumptions.

The nonfatal endpoints included in our analysis are chronic conditions that we assumed would continue for the remainder of the individual's life span. To determine remaining life expectancy with and without each of these conditions, we applied conditional survival rates, based on estimated annual mortality rates for each year of age for the year 2000 (CDC 2003). These survival rates are conditional in that the rate for each year reflects the probability of surviving through the previous years, as illustrated in Appendix B. The calculations were based on the following equation:

$$\text{Conditional survival rate for current year} = \text{survival rate for prior year} * (1 - \text{current year death rate})$$

Our application of these conditional survival rates depended on the health endpoint; the calculations of duration and survival were relatively straightforward for chronic bronchitis, but more complicated for the various post-AMI scenarios.

- C For chronic bronchitis, we assumed that the condition begins on average at age 49 and continues throughout the individual's lifespan, with no reduction in life expectancy.<sup>21</sup> We apply age-specific population average conditional survival rates to these cases.
- C For AMI hospitalization, we assumed an average length of stay of 5.5 days, based on data from the Health Care Utilization Project (HCUP) as reported in Hubbell (2004). The age

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<sup>19</sup> The rationale for this approach is discussed in Hubbell (2004, pp. 8-13) and EPA (2005, p. G-16). Hubbell (2004) also includes sensitivity analyses assuming that deaths occur among those with pre-existing conditions.

<sup>20</sup> This adjustment was not made for infant deaths, which are estimated based on a different risk study and assumed to occur in the same year as the pollution reduction.

<sup>21</sup> Hubbell (2004, p. 14) and EPA (2005, p. G-22) assume that chronic bronchitis will shorten life expectancy by 4.26 years for individuals under the age of 75, and by a corresponding ratio for individuals over the age of 75, based on CDC data on the effect of chronic lower respiratory disease on potential life years lost for individuals under the age of 75. We do not use these data in this case study because they reflect the effects of a number of other respiratory conditions on life expectancy rather than solely the effects of chronic bronchitis.

of incidence was 68 when averaged across all cases, or 53 for those experiencing the AMI before age 65 and 78 for those experiencing the AMI at age 65 or older.

- C For the 20 percent of AMI survivors expected to experience congestive heart failure (with or without angina), we used fixed estimates of remaining life expectancy derived from data reported by Hubbell (2004, Table 9), based on Vos (1999), rather than estimates of conditional survival rates.<sup>22</sup> We assumed that remaining life expectancy was two years if averaged over all AMI survivors, or four years for those who experience the AMI before age 65 and two years for those experiencing the AMI at age 65 or higher. (The average is the same for all cases as for those age 65 and higher because most of the cases averted are among this older age group.)
- C For the 80 percent of AMI survivors who do not experience congestive heart failure, with or without angina, we used the same standardized mortality ratio (SMR) of 1.52 as provided in Hubbell (2004). (SMRs represent the ratio of deaths in the ill population to deaths in the general population.) This SMR was reported in Ganz et al. (2000) based on work by Goldberg et al. (1998). We applied this SMR using an exponential approach starting at the average age of incidence, as illustrated in Appendix B.

For all health endpoints (including preventable mortality), we compared these “with condition” survival rate calculations to population average survival rates by age to determine the impact of each condition on longevity. Consistent with Hubbell (2004, p. 16) and EPA (2004, p. 9-139), we assumed that the years lost to mortality from cardiac disease are included in the separate estimates of fatal cases and should not be assessed as part of the cardiac disease scenario to avoid double-counting. Hence the reduction in HRQL associated with the nonfatal endpoints is assessed only for the affected individuals’ remaining life spans.

The assumptions regarding age, duration, and life expectancy are summarized below.

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<sup>22</sup> We use these averages as fixed estimates rather than conditional survival rates because the remaining life expectancy is small and the Hubbell estimates cannot be easily transformed into the types of survival rates used elsewhere in the analysis.

<b>Exhibit 6</b>				
<b>AGE, DURATION, AND LIFE EXPECTANCY</b>				
<b>Health Condition<sup>a</sup></b>	<b>Average Age at Incidence<sup>b</sup></b>	<b>Duration of Condition</b>	<b>Life Expectancy</b>	
			<b>Without condition</b>	<b>With condition</b>
Nonfatal chronic bronchitis, adults, 26 and over	49	Remaining life span	Annual conditional survival rates, based on U.S. population average mortality rates by year of age	No change
Nonfatal acute myocardial infarction, adults, 18 and over	68 <sup>c</sup>	Remaining life span		Reduced <sup>d</sup>
Particulate matter related mortality – adults, 30 and over	74	N/A		N/A <sup>e</sup>
Particulate matter related mortality – infants under 1 year	0	N/A		N/A
Notes: a. Health condition descriptions are from the nonroad rule analysis (see Exhibit 2 above). b. Calculated based on Hubbell (2004), Tables 2, 6, and 8. c. We subdivide the AMI cases into two categories, depending on whether the AMI occurs before or after age 65. The average age at incidence for the under 65 age group is 53; for those 65 and over, the average is 78. d. For nonfatal AMI without congestive heart failure, we apply a standardized mortality ratio of 1.52 as reported in Ganz et. al (2000), using the approach described in Appendix B. We separately estimate HRQL impacts for congestive heart failure, based on Hubbell (2004, Table 9). In these latter cases, we assume a fixed remaining life span averaging two years across all cases, or four years for those who experience the AMI before age 65 and two years for those experiencing the AMI at age 65 or higher. e. For some cases, there will be a lag between reduced exposure and reduced risks of mortality. Consistent with EPA's analysis of the nonroad rule, we assume that 25 percent of the averted cases of adult mortality would occur in the same year as the pollution reduction, 25 percent in the second year, and 16.7 percent in each of the three following years (EPA 2004, p. 9-23). No lag is assumed for infant mortality.				

### 3.1.2 Comparison to “Without Condition” HRQL

For each of the nonfatal health conditions described above, we used the approaches described in Sections 3.2, 3.3, and 3.4 below to assess HRQL with the illness. We then compared these estimates to estimates of HRQL without the condition (i.e., “normal” health in the absence of the pollution) to determine the HRQL decrement, and multiplied this decrement by the duration of the condition to estimate the QALY losses averted by the rule. For mortality, we compared the “with condition” value of zero to the estimates for normal health. These calculations are introduced below.

After estimating HRQL with each condition under each valuation approach, we compared the resulting values to normal health under two different scenarios: the first assumed that the affected individuals would be in average health for their age in the absence of the condition, the second assumed that they would be in perfect or optimal health throughout their life span (i.e., a value of 1.0). These comparisons involved adjustments to the “with condition” HRQL estimates in some cases, which varied depending on the underlying data source; we discuss these adjustments in the sections describing each HRQL approach.

To estimate average population health by age in the absence of each condition, we relied on unpublished analyses for the EQ-5D and Health Utilities Index Mark 3 (HUI-3) from the following sources.

- C EQ-5D: Dr. William Lawrence, Agency for Healthcare Research and Quality (AHRQ), provided estimates of average HRQL by age and gender, based on 2001 MEPS data. These data represent roughly 19,000 - 20,000 surveys provided by 22,500 eligible respondents. Lawrence provided estimates by gender and age, divided into 10-year age groups beginning with ages 20-29 and ending at ages 80-89.<sup>23</sup> The values reflect community weights from a representative U.S. national sample, derived using the time trade-off elicitation method (Shaw et al., 2005).<sup>24</sup>
- C HUI-3: Average HRQL estimates by age and sex for the HUI-3 were provided by Barbara Altman, National Center for Health Statistics (NCHS) based on data from the Joint U.S.-Canada Survey of Health, 2002-2003, representing a U.S. sample of roughly 5,000 individuals. Altman provided estimates by gender and age, divided into 10-year age groups from ages 20-29 to ages 70-79, as well as the 80-85 age group.<sup>25</sup> The standard HUI-3 values were derived using a multiattribute utility function based on a community sample of residents in Ontario, Canada (Feeny et al., 2002, Table 3).

While most of the analysis in this case study relies on the EQ-5D, we include the HUI because it is used in one of the studies applied in the transfer of estimates from the Harvard CEA Registry.

In Exhibit 7, we provide the estimates of “without condition” or normal health used in this analysis for selected ages, for males and females combined. We weighted the gender-specific values for each index by the proportion of males and females of each age in the U.S. general population as of the year 2000, to determine population averages (Census 2004). The exhibit reports the values for only a few ages for illustrative purposes; the case study calculations use the full range of age-specific estimates provided. The source documents cited provide information on the confidence intervals associated with the gender-specific estimates and on the uncertainty associated with each generic instrument and its set of community weights.

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<sup>23</sup> Email from William Lawrence to Wilhelmine Miller, November 9, 2004.

<sup>24</sup> Updated EQ-5D estimates are available in Hamner et al., forthcoming.

<sup>25</sup> Email from Barbara Altman to Wilhelmine Miller, January 7, 2004.

<b>Exhibit 7</b>				
<b>HRQL IN THE ABSENCE OF PM-RELATED ILLNESS</b>				
	<b>Age 20</b>	<b>Age 40</b>	<b>Age 60</b>	<b>Age 80</b>
<i>Mean Population HRQL Index Value (base case)</i>				
EQ-5D	0.921	0.875	0.825	0.746
HUI-3	0.908	0.880	0.822	0.694
<i>Perfect HRQL (sensitivity analysis)</i>				
All indices	1.0	1.0	1.0	1.0
Notes: Estimates are preliminary; see Hamner et al. (forthcoming) for updated EQ-5D estimates. See sources below for information on the confidence intervals related to each of these estimates. Additional uncertainty related to the EQ-5D and HUI-3 instruments and valuation surveys is discussed in the sources describing their development. Sources: EQ-5D: Unpublished analysis by William Lawrence, November 9, 2004 HUI-3: Unpublished analysis by Barbara Altman, January 7, 2005.				

As is evident from the exhibit, the estimates of average population health vary across the two indices used in this case study. This variation reflects several factors, including the differences in: (1) the data sources used to assess health attributes; (2) the sources of community weights used to value these attributes; and (3) the indices themselves. Which index leads to higher estimates of average HRQL varies by age, although the EQ-5D values are often greater than the HUI estimates especially for the youngest and oldest age groups illustrated. As expected, average HRQL declines with age under both indices.

These EQ-5D and HUI analyses are missing average population health estimates for the very young and the very old. We assumed that average health would equal perfect health (1.0) for ages 0 to 9, and that the value from age 10 to 19 would be the mid-point between perfect health and the values estimated for ages 20 to 29. For elderly individuals, we assumed that the HRQL would remain constant throughout their remaining life span at the value reported for the eldest age group.

The final step in the analysis involved multiplying the decrement that results from the comparison of with- and without-condition HRQL by the duration of each condition, to determine the resulting QALY losses. Because we assumed that both chronic bronchitis and cardiac disease have life-long impacts, this calculation involves multiplying the change in HRQL by the estimates of life expectancy discussed in Section 3.1.1. For preventable mortality, the losses are equal to a loss of total HRQL over the remaining life span.

## 3.2 Expert Assignment of EQ-5D Attributes

The first HRQL assessment completed for this case study involved asking clinical experts to match the descriptions of the selected health conditions with the appropriate attribute descriptions under the EQ-5D, then estimating the resulting HRQL based on the standard weighting formula for this index.<sup>26</sup> Because HRQL is zero following mortality, the experts were only asked to consider the nonfatal endpoints (the disease states associated with chronic bronchitis and cardiac disease following a nonfatal AMI), but we include preventable mortality in our calculations of QALY losses. In the following sections, we discuss the detailed disease descriptions developed for the expert process, describe the process itself, and then summarize how we translated the results into estimates of the QALY losses averted by the regulations.

### 3.2.1 Detailed Disease Descriptions

The starting point for the disease descriptions sent to the medical experts was the definitions included in the risk studies underlying EPA's analysis of the impacts of the nonroad rule, as summarized in Section 3.1.1 above. For the expert assignment process, we divided the nonfatal effects into subcategories based on severity, rather than asking the experts to determine the attributes of an average or typical case across all severity categories. Below, we discuss the descriptions developed for each nonfatal health state assessed. As noted in the section on limitations, we were not able to pre-test these descriptions given the time and budget constraints.

***Chronic bronchitis:*** As discussed earlier, EPA's estimates of new cases of chronic bronchitis averted by the regulations were based on work by Abbey et al. (1995). In an initial, more detailed report on this research, Abbey subdivided the cases of chronic bronchitis into six grades, based on the frequency of cough, the frequency of sputum production, and the extent to which the individual experienced shortness of breath (Abbey 1994). Grade 0 indicated that there were no symptoms, grade 1 indicated infrequent symptoms that could represent a possible case of chronic bronchitis, and grades 2 through 5 represented definite cases with symptoms of increasing severity. We focused on grades 2 through 5, since these represent the definite cases included in the risk estimates applied by EPA. Exhibit 8 presents the definitions used for each category, as well as the percentage of all cases (not solely those attributed to air pollution) that fell into each category. We apply these percentages in our analysis.

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<sup>26</sup> We used an expert assignment process rather than surveying patients due to the limited time and resources available.

<b>Exhibit 8</b>			
<b>CATEGORIZATION OF CHRONIC BRONCHITIS CASES IN ABBEY (1994)</b> <b>(definite cases only)</b>			
<b>Grade</b>	<b>Cough Symptoms</b>	<b>Sputum Symptoms</b>	<b>Percent of Cases</b>
<b>2</b>	Cough first thing in morning OR cough at other times AND cough on most days for 3 months or more	Sputum first thing in morning OR sputum at other times AND sputum on most days for 3 months or more	23.6 percent
<b>3</b>	Cough first thing in morning AND cough at other times AND cough on most days for 3 months or more	Sputum first thing in morning AND sputum at other times of day AND sputum on most days for 3 months or more	23.9 percent
<b>4</b>	Cough first thing in morning OR cough at other times AND cough on most days for 3 months or more AND shortness of breath with light to moderate activity AND no shortness of breath with normal walking	Sputum first thing in morning OR sputum at other times AND sputum on most days for 3 months or more AND shortness of breath with light to moderate activity AND no shortness of breath with normal walking	31.0 percent
<b>5</b>	Cough first thing in morning OR cough at other times AND cough on most days for 3 months or more AND shortness of breath with normal walking	Sputum first thing in morning OR sputum at other times AND sputum on most days for 3 months or more AND shortness of breath with normal walking	21.6 percent
<b>Total, Definite Cases</b>			100.0 percent
<p>Source: Abbey (1994), Appendix B, Table 1, pp. B-2 to B-3, and Exhibit 1, pp. B-7 to B-9.</p> <p>Notes:</p> <p>Detail does not add to total due to rounding.</p> <p>Grades represent categories used in the Abbey analysis for definite cases of chronic bronchitis; these subcategories were not used in the nonroad rule analysis, which includes a single estimate for all averted cases of chronic bronchitis (see Exhibit 2).</p> <p>Percentage of cases calculated based on reported results for 1987, combining data for cough and sputum cases, and including all cases (not solely those potentially attributable to air pollution).</p>			

EPA’s analysis of the impacts of the nonroad rule does not use these subcategories (rather, it uses a single impact function that combines all of these grades) and addresses statistical cases rather than individual, identifiable patients.<sup>27</sup> However, we used these grades in developing descriptions for the expert elicitation process. Asking the experts to identify the average EQ-5D attribute scores for the typical chronic bronchitis patient over time presents a number of cognitive challenges. By providing the experts with descriptions of different severity levels, we hoped to ease the burden associated with this exercise.

<sup>27</sup> As noted earlier, “statistical cases” refers to two inter-related aspects of the risk assessment often used to support regulatory analysis: (1) it reflects predicted changes in the risks of incurring a condition throughout a large population and (2) the particular individuals likely to be affected are not identifiable.

We consulted with respiratory disease experts at the Centers for Disease Control (CDC) and Prevention to determine how to best present this information.<sup>28</sup> Based on their advice, we simplified the categories used by Abbey and defined three severity levels, as presented in Exhibit 9. We assumed that the cases we describe as mild generally correspond to those in Abbey’s Grade 2 (23.6 percent of the total), moderate correspond to Abbey’s Grades 3 and 4 (54.8 percent), and severe to Abbey’s Grade 5 (21.6 percent).

<b>Exhibit 9</b>	
<b>CHRONIC BRONCHITIS DISEASE DESCRIPTIONS USED IN EXPERT ASSIGNMENT</b>	
<b>Disease Description</b>	<b>Percent of Cases</b>
<i>Mild Chronic Bronchitis:</i> No difficulty breathing, or difficulty only with strenuous activities such as running; unaware of coughing, or coughing rarely; no difficulty with sputum or sputum rarely caused a problem.	23.6 percent
<i>Moderate Chronic Bronchitis:</i> Difficulty breathing noticeable during light activity such as bed making; occasional cough, less than hourly; sputum noticeable as a problem.	54.8 percent
<i>Severe Chronic Bronchitis:</i> Difficulty breathing noticeable when washing or dressing or almost constant, even when resting; cough once or twice an hour to almost constant, i.e., never free of cough or need to cough; sputum is marked, causing a great deal of inconvenience to almost a constant problem.	21.6 percent
Total	100.0 percent
Note: Detail does not add to 100 percent due to rounding. Unrounded results are used in all calculations.	

We further instructed the experts to assume that the patient is in middle age, and noted that patients with only some of the listed symptoms should be categorized by the symptom that places them in the most severe scenario. For example, a patient with constant sputum problems but occasional cough would be placed in the severe category, while a patient with only an occasional cough would be placed in the moderate category.

***Nonfatal AMI and subsequent progression of cardiac disease:*** For AMI, the development of disease descriptions was more complicated. Our starting point was the study EPA used in the nonroad rule analysis (Peters et al., 2001), supplemented by information from Hubbell (2004) as discussed in Section 3.1.1. However, we determined that further sub-categorization was needed for the expert assignment process, due to the difficulties inherent in estimating impacts for an average or typical case when the disease can vary greatly in severity.<sup>29</sup> We used severity classes developed by the New York Heart Association (NYHA) and also

<sup>28</sup> The disease descriptions for chronic bronchitis were developed by Seymour Williams and Fernando Holguin of CDC, based largely on Leidy et al. (2003). Note that the typical classification of such cases has changed since the Abbey study was completed; chronic bronchitis is now usually subsumed under the general category of chronic obstructive pulmonary disease.

<sup>29</sup> The disease descriptions for cardiovascular conditions were developed with the assistance of Milton Weinstein of the Harvard Center for Risk Analysis.

separated cases by age at incidence to reflect differences in the likely HRQL impacts. Consistent with Hubbell (2004) and EPA (2005), we assumed that angina symptoms would be treated and hence would be mild or moderate. In addition, the experts were not asked to assess cases where neither congestive heart failure or angina was expected to follow the nonfatal AMI; in these cases we assumed that the patient returns to normal health following the event.<sup>30</sup>

We assumed that all patients experience the hospitalization period, and allocated the cases across the various post-hospitalization categories using the percentages reported in earlier Exhibit 5. Within these categories, we divided the cases evenly across the relevant NYHA classes. Cases were allocated to the above- and below-age 65 age groups based on age at incidence data reported in Hubbell (2004, Table 8). The resulting disease descriptions and allocation of cases is provided in Exhibit 10.

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<sup>30</sup> Our approach for assessing normal health involves two comparisons, one to average age-adjusted health and one to perfect health, as discussed in Section 3.1.2.

<b>Exhibit 10</b>	
<b>CARDIOVASCULAR DISEASE DESCRIPTIONS USED IN EXPERT ASSIGNMENT</b>	
<b>Disease Description<sup>a</sup></b>	<b>Percent of Cases</b>
Hospitalization period for non-fatal myocardial infarction	100 percent
<i>Post-hospitalization effects of cardiac disease assuming:<sup>b</sup></i>	
Class I angina only	20.4 percent
Class II angina only	20.4 percent
Class I congestive heart failure only	2.5 percent
Class II congestive heart failure only	2.5 percent
Class III congestive heart failure only	2.5 percent
Class IV congestive heart failure only	2.5 percent
Class I congestive heart failure with mild or moderate angina	2.6 percent
Class II congestive heart failure with mild or moderate angina	2.6 percent
Class III congestive heart failure with mild or moderate angina	2.6 percent
Class IV congestive heart failure with mild or moderate angina	2.6 percent
Total, post-hospitalization (excludes 39.2 percent of cases without congestive heart failure or angina)	60.8 percent <sup>c</sup>
<p>Notes:</p> <p>a. Each endpoint was assessed separately for patients experiencing the nonfatal AMI at ages less than 65 and at ages 65 or older.</p> <p>b. Classification system refers to the following definitions developed by the New York Heart Association (<a href="http://www.americanheart.org/presenter.jhtml?identifier=4569">http://www.americanheart.org/presenter.jhtml?identifier=4569</a>):</p> <p><b>Class I.</b> Patients with cardiac disease but without resulting limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea or anginal pain.</p> <p><b>Class II.</b> Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea or anginal pain.</p> <p><b>Class III.</b> Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea or anginal pain.</p> <p><b>Class IV.</b> Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart failure or the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort increases.</p> <p>c. Percentages for post-hospitalization period reflect allocation of conditions from Hubbell (2004) as reported in Exhibit 5 above, and do not add to 100 percent due both to rounding and to exclusion of the 39.2 percent of cases expected to not result in congestive heart failure or angina. Unrounded numbers are used in all calculations.</p>	

### 3.2.2 Expert Assignment Process

To identify experts to participate in this task, we worked through the case study team’s professional contacts.<sup>31</sup> We developed two groups, one to assign attributes to the chronic

<sup>31</sup> These experts were identified by Wilhelmine Miller with assistance from Seymour Williams and Fernando Holguin of CDC and consultants from Industrial Economics, Incorporated (IEc) for the respiratory experts, and from Darwin LaBarthe of CDC for the cardiologists. Note that we selected these experts based largely on the extent and relevance of their clinical expertise and their willingness to participate in this assessment on short notice. As discussed later in the section on limitations, for

bronchitis endpoints in Exhibit 9 and a second to assign attributes to the cardiovascular endpoints in Exhibit 12. The experts are listed in Exhibit 11 below.

<b>Exhibit 11</b>	
<b>CLINICAL EXPERTS</b>	
<b>Respiratory Disease</b>	<b>Cardiovascular Disease</b>
1. David M. Mannino, M.D., University of Kentucky School of Medicine 2. Peter Barkin, M.D., Emerson Hospital 3. R. Graham Barr, M.D., Presbyterian Hospital, Columbia University 4. Scott D. Ramsey, M.D., Fred Hutchinson Cancer Research Center 5. Mark J. Utell, M.D., University of Rochester 6. Roger Yusen, M.D., Washington University School of Medicine	1. Harlan M. Krumholz, M.D., Yale Medical School 2. Russell V. Luepker, M.D., Mayo Clinic 3. John Rumsfeld, M.D., University of Colorado 4. Douglas D. Schocken, M.D., University of South Florida 5. John Spertus, M.D., University of Missouri-Kansas City

Members of the case study team contacted each expert by phone or email to describe the project and determine whether the expert was interested and available to participate. We then sent each expert a package of materials that included a cover letter providing detailed instructions, sheets defining the attributes within each domain for the EQ-5D index, and a table containing the health state descriptions (from Exhibits 9 and 10) that included space to fill in the relevant attribute values. A copy of the cover letter sent to each expert appears below.<sup>32</sup> The EQ-5D domains and attributes are provided in Appendix C to this report.

<b>Exhibit 12</b>
<b>INSTRUCTIONS SENT TO CLINICAL EXPERTS</b>
<p>February 24, 2005</p> <p>Dear _____:</p> <p>Thank you for agreeing to participate in the development of a case study for the Institute of Medicine’s (IOM) <i>Committee to Evaluate Measures of Health Benefits for Environmental, Health, and Safety Regulation</i>. In collaboration with economists and environmental health experts at CDC, we are converting a benefit-cost analysis developed by the EPA for an air quality improvement rule, emission standards for non-road diesel engines, into a cost-effectiveness analysis of the health benefits of the rule.</p> <p>As such, we are trying to “value” certain health conditions affected by reductions in particulate matter (PM<sub>2.5</sub>) concentrations in quality-adjusted life years (QALYs), using different approaches to estimating QALYs. We would like your help with one of these valuation exercises, which involves describing the health-related quality of life (HRQL) aspects of each health condition using a generic HRQL survey instrument, the EuroQol EQ-5D. The EQ-5D is a patient or self-report questionnaire with five questions that address the domains of mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, with three possible level</p>

regulatory analyses it may be desirable to consider other criteria (such as the range of subspecialties and geographic locations) since these considerations are likely to affect the characteristics of the patients seen and conditions examined.

<sup>32</sup> This letter was developed with assistance from Adam Atherly and Tursynbek Nurmagambetov of CDC.

## Exhibit 12

### INSTRUCTIONS SENT TO CLINICAL EXPERTS

responses for each domain. Although the EQ-5D survey instrument was originally intended for completion by individuals assessing their own health, we are using physician experts as “patient proxies,” for this illustrative exercise.

As one of several experts in respiratory [*cardiovascular*] disease, we would like you to characterize the health-related quality of life of persons with chronic bronchitis [*...who have survived a nonfatal myocardial infarction*] by filling out the EQ-5D survey for the “typical” patient with the condition at each of three severity levels, described symptomatically. [*...for each of the clinical scenarios described. These include the period of hospitalization, and post-hospitalization conditions that include either some degree of angina or congestive heart failure, or both. We are not asking you to assess the health-related quality of life for AMI survivors who have neither angina nor congestive heart failure, although they will be accounted for in the analysis.*]

A description of the EQ-5D domains and attribute level descriptions is attached, as is a table with several briefly characterized disease condition scenarios. [*Please assess the average daily experience of the “typical” patient within each scenario for the five domains.*]

When you have completed this assessment, please return your assessments to me, preferably by filling out the attached Excel spreadsheet electronically and emailing it back. You will also receive this letter and attachments in hard copy format, and you are welcome to fill out the tables by hand and send them back in the self-addressed pre-paid envelope provided if that is more convenient.

Once we have received your and your colleagues’ answers, we will be able to apply HRQL weights (on a scale from 0 to 1, where 0 is death and 1 is perfect health) associated with the set of responses across all domains for a given scenario. The weights for the EQ-5D are based on a nationally representative sample of U.S. adults. This final step will allow us to assess the loss in HRQL in terms of quality-adjusted years of life predicted by the EQ-5D.

We would appreciate receiving your completed form by March 4, 2005. If you have any questions, please contact me by phone (202-334-1359), by fax (202-334-2862) or by email ([wmillers@nas.edu](mailto:wmillers@nas.edu)). Additionally, if you have comments on how this process might be revised if we were to repeat it or other reactions to this expert assessment exercise, please forward them along with the tables. With your permission, I would like to call you at your convenience for a short debriefing interview after you have completed the assessment.

Again, thank you very much for your time and for contributing your invaluable expertise to the development of this case study. We expect to have a draft version of the case study completed by May 2005 and will be glad to send you the results of the expert panel assessment exercise at that time, and a copy of the final IOM report including the completed case studies once the report is published. Your contribution will be acknowledged in the IOM report. If you have any questions about this project or about this specific task, please do not hesitate to contact me.

Sincerely,

Wilhelmine Miller, M.S., Ph.D.

Attachments

Notes:

Regular text represents letter sent to respiratory specialists, *italicized* text represents changes incorporated into the version sent to the cardiologists. Actual letter was printed on IOM letterhead.

Once we received the completed tables from the experts, we incorporated them into an Excel spreadsheet model used to assess the HRQL impacts associated with each health state, as discussed in more detail below.<sup>33</sup>

<sup>33</sup> These spreadsheets were developed by Committee consultant Robert Black, with assistance from Jim Neumann and Sarah Brennan of Industrial Economics, Incorporated (IEc). Jim DeMocker of EPA supported IEc’s involvement in this exercise.

Because the purpose of this exercise was to educate the Committee about the challenges inherent in applying HRQL approaches in regulatory analyses and was conducted with limited time and resources, we followed a simplified expert assignment process that does not necessarily follow the practices that might be appropriate in the context of regulatory analysis. For example, we did not work with the experts to ensure that they had a thorough or common understanding of the materials describing the health states, the domain attributes, or the task itself. In addition, we did not attempt to resolve any inconsistencies or to achieve consensus across the experts. The implications of this simple, abbreviated expert elicitation process, as well as comments on the process received from the experts themselves, are discussed in Section 5.0 of this report.

### 3.2.3 Estimates of QALY Losses

As described above, the expert judgment process involved taking the disease descriptions discussed in Section 3.2.1 and locating them according to the domain attribute levels listed in Appendix C (e.g., mobility = 1, self-care = 2, etc.). Using these domain attributes to assess the QALY losses associated with each health condition involves three additional steps.

1. Transforming the results of the expert assignments into estimates of HRQL with each health condition; i.e., HRQL with chronic bronchitis or cardiac disease.
2. Comparing these values to HRQL in the absence of the condition, to determine the HRQL decrement attributable to the condition.
3. Multiplying the resulting decrement by the duration of the condition to estimate the QALY losses.

We introduced our approach to this part of the analysis previously in Section 3.1.2. Below, we discuss how we completed each of these steps for the expert assignments.

**Step 1 -- Determine HRQL with the condition:** The expert assignment process discussed above provided descriptive information on the HRQL impacts of each health condition; for example, on the extent to which the condition limits mobility. To determine the value of these attributes (i.e., individuals' relative ranking of these effects, or their willingness to trade-off perfect health against these impacts), we weighted the attributes using the standard EQ-5D formula. These weighted values are on a zero to one scale, where zero corresponds to death and one corresponds to perfect health.<sup>34</sup> For the EQ-5D, these weights were derived from a representative U.S. national sample, using a survey that employed the time trade-off elicitation method (Shaw et al., 2005).<sup>35</sup>

**Step 2 -- Compare to HRQL without the condition, and calculate the decrement:** We then compared the values that resulted from Step 1 to normal health under two scenarios: the first assumed that the affected individuals would be in average health for their age in the absence of the condition, the second assumed that they would be in perfect health (a value of 1.0) for the remainder of their life time. The comparison of HRQL with the condition to perfect health was

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<sup>34</sup> Negative values are possible in cases where the combination of attributes is weighted at less than zero.

<sup>35</sup> Dr. William Lawrence, AHRQ, provided the spreadsheet used to apply these weights.

straightforward; we simply subtracted the weighted HRQL results (from Step 1) from a value of 1.0 to determine the difference. For average age-adjusted health, the comparison was more complex.

Many researchers believe that individuals responding to the sorts of questionnaires used in the expert assignment process implicitly compare the condition to perfect health, rather than to average health for an individual of a given age. The case study team discussed several approaches for anchoring the expert responses in average age-adjusted health; e.g., by providing information on the domain attributes likely to be associated with typical health at selected years of age. However, we determined that these approaches were too complex to implement in the simple expert judgment process used for this case study. Instead, we decided to adjust the “with condition” HRQL results proportionately when comparing them to average health.<sup>36</sup>

More specifically, the starting point for the average health comparisons was the age-adjusted estimates of population health developed by Dr. William Lawrence, as discussed in Section 3.1.2. In applying these estimates, we multiplied the weighted EQ-5D value for the health condition by the average population HRQL for the same age group, then used this adjusted result in our analysis. This calculation is equivalent to assuming that the “with condition” HRQL is the same proportion of both average health and perfect health.<sup>37</sup> For example, if the expert assignment results in a HRQL value of 0.8 for the health condition, it would be equivalent to 80 percent of perfect health. If the average population HRQL is 0.9 for the same age, the “adjusted” HRQL for that condition (in comparison to average health) would be 0.72 ( $0.8 * 0.9$ ). The decrement is then equal to the average health estimate minus the adjusted “with condition” value; i.e., 0.18 ( $0.9 - 0.72$ ). In contrast, the decrement from perfect health would be 0.2 ( $1.0 - 0.8$ ). Thus our approach assumed that each expert was comparing the condition to perfect health, and, that if they had instead compared to age-adjusted average health, the estimate of HRQL with the condition would reflect the same proportionate reduction. We recognize that this is a somewhat imperfect approach to addressing this issue, but it was the most pragmatic option in the context of the case study.

***Step 3 – Multiply the decrement by duration to assess QALY losses:*** The final step involved multiplying the decrement (that results from the comparison in Step 2) by the duration of each health condition, to determine the QALY losses attributable to the condition. Because we assume that both chronic bronchitis and cardiac disease have life-long impacts, this calculation involves multiplying the difference between the with- and without-condition HRQL for each year of age, based on the life expectancy assumptions discussed in Section 3.1.2. For preventable mortality, the losses are calculated assuming that life expectancy would have otherwise equaled the average for the U.S. population as discussed earlier.

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<sup>36</sup> This approach is based on a suggestion from Judith Wagner and discussions with Committee members Dennis Fryback, Alan Garber, Marthe Gold, and Emmett Keeler.

<sup>37</sup> Because the “with condition” value is on a scale of zero to one, we did not need to first translate it into a percentage before doing this calculation.

### 3.3 Application of Medical Expenditure Panel Survey EQ-5D Weights

The second HRQL approach used in this case study involved applying EQ-5D decrements from a catalogue of chronic condition weights developed by Sullivan et al. (2005). Below, we introduce this study and describe its application, referring back to the previous sections for those aspects of the analysis that used the same approach as applied elsewhere in this case study.

Sullivan et al. (2005) used the Medical Expenditure Panel Survey (MEPS) to develop EQ-5D weights for a number of chronic conditions, based on pooled data for the years 2000 and 2001 for respondents aged 18 or older. MEPS includes data on sociodemographic characteristics as well as responses to the EQ-5D health status questionnaire; valid responses were received for about 29,000 individuals. (The EQ-5D domain and attribute descriptions reflected in this questionnaire are provided in Appendix C of this case study.) The researchers weighted the resulting attribute scores based on the same research on U.S. community preferences (Shaw et al., 2005) that we applied in the expert assignment process (see Section 3.2) and that were used to estimate average population health (see Section 3.1.2).

The researchers then calculated mean EQ-5D condition values for those respondents reporting each condition. These “with condition” values reflect both the condition itself and any co-morbidities, indicating the overall health of the individual. To separate out the effects of these co-morbidities, the researchers then used regression analysis to determine the marginal impact of the condition of interest alone, calculated as a decrement from median population health. These marginal decrements in EQ-5D values exclude the effects of age, gender, race, ethnicity, income, and education as well as co-morbidities. The marginal decrements can be added across conditions. In their article, Sullivan et al. report the results for clusters of chronic conditions of particular interest to health care researchers. Estimates for individual conditions (by three digit International Classification of Disease Version 9 (ICD-9) codes) are also available from the study authors. It is important to note, however, that this case study relies on preliminary results from this research; the published version of the study provides somewhat different weights and a different process for applying them.

To apply these decrements to the nonfatal health conditions assessed in this case study, we again began with the information on disease characteristics contained in the studies selected by EPA to estimate the risks of chronic bronchitis (Abbey et al., 1995) and AMI (Peters et al., 2001), as discussed in Section 3.1.1.<sup>38</sup> We used the same assumptions regarding disease progression and duration as in the expert assignment, applying the percentages reported in Exhibit 5 to estimate the fraction of AMI survivors likely to experience congestive heart failure and/or angina, and the approaches summarized in Exhibit 6 to assess age at incidence, duration, and life expectancy with and without each condition.

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<sup>38</sup> As before, the “with condition” value of preventable mortality is zero, and the estimates of cases averted are based on Pope et al., 2002.

Application of the Sullivan et al. weights did not require development of detailed disease descriptions, however. Instead, we identified the ICD-9 codes associated with each condition.<sup>39</sup> Sullivan then provided a spreadsheet that contained the preliminary values of interest.<sup>40</sup> These values are reported below.

<b>Exhibit 13</b>					
<b>PRELIMINARY EQ-5D CATALOGUE RESULTS FOR CHRONIC BRONCHITIS AND SELECTED CARDIAC CONDITIONS</b>					
<b>ICD-9 Code</b>	<b>Description</b>	<b>Number of Respondents</b>	<b>Average Age</b>	<b>Mean HRQL with Condition* (25<sup>th</sup> and 75<sup>th</sup> percentiles)</b>	<b>Decrement from Median HRQL** (Standard Error)</b>
491	Chronic bronchitis	72	52	0.7493 (0.7077, 0.8271 )	-0.06521 (0.01135)
410	Acute myocardial infarction	244	62	0.7042 ( 0.5753, 0.8432 )	-0.04008 (0.006634)
413	Angina pectoris	229	68	0.6956 (0.5165, 0.8271 )	-0.03652 (0.006518)
428	Heart failure	284	71	0.6356 ( 0.4375, 0.8100)	-0.06980 (0.005794)

Source: Unpublished analysis provided by Patrick Sullivan, April 4, 2005

Notes:  
 Estimates are preliminary; see Sullivan et al. (2005) for final results  
 \* Includes co-morbidities; reflects mean HRQL for individuals reporting the condition.  
 \*\* Excludes co-morbidities; reflects regression results controlling for age, gender, race, ethnicity, income, and education as well as co-morbidities.

As indicated by the exhibit, the MEPS dataset included between 72 and 284 respondents reporting each condition of interest. The average ages of these respondents were similar to the averages used in the EPA analysis; as reported in Exhibit 6, EPA's age distributions lead to an estimated average age at incidence of 49 for chronic bronchitis and 68 for nonfatal AMI. On a zero-to-one scale (with zero corresponding to death and one corresponding to perfect health), the overall HRQL for respondents reporting each condition ranged from about 0.64 to 0.75. However, the decrement in HRQL appears much smaller when regression analysis is used to separate out the effects of co-morbidities and other factors. As a decrement from median population health (which was 0.844 when calculated across all age groups, and includes the entire population regardless of whether they have the conditions of concern), the conditions yielded preliminary values ranging from about 0.037 to 0.070.

<sup>39</sup> The approach for applying the Sullivan weights in this case study was developed based on advice from two of the study authors (Patrick Sullivan and William Lawrence) as well as Committee members and advisors Richard Burnett, Dennis Fryback, Marthe Gold, James Hammitt, and Milton Weinstein, and EPA consultants Jim Neumann and Sarah Brennan of Industrial Economics, Incorporated (IEC). Jim DeMocker of EPA supported IEC's involvement in this effort.

<sup>40</sup> Email from Patrick Sullivan to Wilhelmine Miller, April 4, 2005.

To apply these estimates, we used the same decrement for all cases of chronic bronchitis averted by the rule. For the AMI endpoints, we combined the values as needed for each subcategory (i.e., with or without congestive heart failure or angina). The resulting estimates are provided in the exhibit below.

<b>Exhibit 15</b>		
<b>PRELIMINARY EQ-5D CATALOGUE DECREMENTS FOR EPA HEALTH CONDITIONS</b>		
<b>Health Endpoint</b>	<b>Decrement</b>	<b>Percent of Cases</b>
Chronic bronchitis	-0.06521	100.0 percent
<i>Post-AMI health states:</i>		
Congestive heart failure AND angina	-0.14640 = -0.04008 + -0.06980 + -0.03652	10.2 percent
Congestive heart failure WITHOUT angina	-0.10988 = -0.04008 + -0.06980	9.8 percent
Angina WITHOUT congestive heart failure	-0.07660 = -0.04008 + -0.03652	40.8 percent
WITHOUT congestive heart failure OR angina	-0.04008	39.2 percent
Total		100.0 percent
Sources: See Exhibits 5 and 15. Notes: Estimates are preliminary; see Sullivan et al. (2005) for final results.		

Transforming these estimates into estimates of the QALY losses averted by the rule is straightforward when comparing to age-adjusted population health. We simply multiplied the decrements from Exhibit 14 by the duration of each condition, using the same approach for assessing life expectancy as discussed in Section 3.1.2 and applied to the expert assignment results. The average health estimates used in this calculation are the same as the EQ-5D results used in the expert assignment (illustrated in Exhibit 7) and were calculated from MEPS by one of the Sullivan et al. co-authors.

The comparison to perfect health was more complex. We followed a different approach in this case than in the expert assignment, because the decrements reported are in comparison to median health and are controlled for age. To compare “with condition” health to perfect health, we added the difference between average health and perfect health at each age to the decrement from Exhibit 14.<sup>41</sup> For example, at age 80, average health is 0.746, a decrement of 0.254 from

<sup>41</sup> This approach mixes mean and median values; the Lawrence EQ-5D estimates of age-adjusted population health used in our analysis are means and the Sullivan et al. estimates of decrements are calculated from median population health. Data provided by Sullivan suggests that the relationship

perfect health. For chronic bronchitis, we would add this decrement to the condition-specific decrement (0.065) to determine the total decrement from perfect health ( $0.254 + 0.065 = 0.319$ ). We then multiply this decrement by the duration of the condition to estimate QALY losses. For preventable mortality, our approach is identical to the approach used for the expert assignment; we apply the same EQ-5D estimates to assess the value of the life years lost in both cases.

### 3.4 Transfer of Values from Studies in the Harvard Registry

The third approach used in this case study involved transferring estimates from the Harvard Center for Risk Analysis' CEA Registry.<sup>42</sup> This on-line Registry contains about 1,558 cost-effectiveness ratios from about 539 articles published between 1976 and 2001. The researchers identified these studies through periodic searches of the literature; the studies were then reviewed by trained readers, who extracted summary information to include in the Registry. The Registry includes all identified English language studies that were published in a peer reviewed journal, and include original estimates of costs per QALY for the intervention of interest.

As in the other two HRQL approaches applied in this case study, we began with the information on disease characteristics provided in the studies selected by EPA as the basis of its risk estimates. For the nonfatal endpoints, Brauer and Neumann (2005) searched the registry for studies that addressed these health conditions, and identified 151 health states and preference scores that addressed relevant respiratory and cardiac diseases. They then excluded most studies published prior to 1994, since the resulting values may no longer be relevant given the changes in disease diagnosis and treatment, which left 127 possible values.<sup>43</sup>

Brauer and Neumann (2005) then applied the following criteria to identify those estimates most suitable for application to this case study.<sup>44</sup>

- C First, they assessed the *applicability of the health state*; i.e., the extent to which the description in the published study matched the health condition described in the risk analyses used by EPA. They considered similarities in factors such as the severity of

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between the population median and mean values varies depending on age. For example, the median EQ-5D value for ages 50-64 is 0.83, while the mean is 0.84. For ages 65 and above, the median is 0.81 and the mean is 0.79. Sullivan et al. recommend using median values to the extent possible, but note that the use of means should not introduce significant bias (personal communications between Patrick Sullivan and William Lawrence and Lisa Robinson, March 31 and April 5, 2005).

<sup>42</sup> The approach for selecting estimates from the Harvard Registry is described in Brauer and Neumann (2005). Judith Wagner and Wilhelmine Miller also provided advice related to the use of these estimates. Background information on the Registry is taken from its website (<http://www.hsph.harvard.edu/cearegistry/>), as viewed on April 15, 2005.

<sup>43</sup> These remaining values include one pre-1994 study, which was the only study that provided an estimate for in-hospital AMI.

<sup>44</sup> There is an extensive literature on benefit transfer that provides a number of different types of criteria that could be applied in these contexts; see, for example, OMB (2003), EPA (2000), and Desvousges et al. (1999). For this analysis, we use the criteria developed by Brauer and Neumann specifically for application of the Harvard database to the EPA case study; these criteria are discussed further in the Committee's final report.

disease and the timing and duration of treatment, as well as the characteristics of the target population and its baseline health status. Of the 127 values, they found 55 that appeared to best correspond to the health states used in the EPA analysis, including estimates for differing severity levels or phases of the illness (e.g., in-hospital AMI) as well as estimates that apply more broadly across a range of types of cases of each illness.

- C Second, they assessed the *appropriateness of the methodology* used to elicit the preference weights, considering the type of population surveyed, the elicitation technique, and size of the sample. Related criteria were based largely on the recommendations of the Panel on Cost-Effectiveness in Health and Medicine (Gold et al., 1996).

-- For the source of the health state values, they favored weights elicited from community samples; weights elicited from patients were ranked next, followed by those elicited from authors or experts in the field.

-- For HRQL measurement, they prioritized values from generic instruments (such as the EQ-5D or HUI) over those elicited through a direct time-trade-off or standard gamble approach. For other directly-elicited weights, they ranked those elicited by a rating scale technique over those derived without any formal methodology from clinicians, other experts, or author judgment. Values from studies that did not specify the methodology used were ranked last.

-- For sample size, larger sample sizes were preferred to smaller ones.

Based on these criteria, Brauer and Neumann (along with other members of the case study team) reviewed the available studies and identified two that appeared to provide the best match to the nonfatal endpoints as defined in the risk studies used by EPA. These studies are summarized in Exhibit 15 below; the range of estimates from other studies of these endpoints are reported in Brauer and Neumann (2005) and summarized in Section 5.0 of this paper.

<b>Exhibit 15</b>				
<b>SELECTED HARVARD REGISTRY ESTIMATES FOR CHRONIC BRONCHITIS AND NONFATAL AMI<sup>a</sup></b>				
<b>Health Endpoint</b>	<b>Study</b>	<b>Population Sampled (sample size)</b>	<b>Index</b>	<b>HRQL Estimate (standard deviation)</b>
Chronic bronchitis	Torrance et al. (1999) <sup>b</sup>	Outpatients with acute exacerbations of chronic bronchitis in Ontario and Quebec, Canada during 1993-1994 (240 adults age 18 and over)	HUI- 3	Ciprofloxacin: 0.79 (0.16) Usual care: 0.76 (0.17) <sup>c</sup>
Nonfatal AMI	Oostenbrink et al. (2001)	Patients with peripheral vascular disease in the Netherlands during 1995-1998 (2,650 patients)	EQ-5D	Post-AMI: 0.58 (N.R.) <sup>d</sup>
Notes: a. Based on review of selected studies from the Harvard Registry by Carmen Brauer, Peter Neumann, and Wilhelmine Miller. See text for discussion of alternative values for these endpoints. b. This research was originally reported in Grossman et al. (1998). c. We use a weighted average of these values (0.78) in the analysis. d. N.R. = not reported.				

For chronic bronchitis, we relied on estimates from a Canadian study of alternative treatments for patients with acute exacerbations (Torrance et al., 1999). The patients studied had an average age of about 55, compared to an average of 49 from EPA’s analysis. Most patients (almost 75 percent) had chronic bronchitis symptoms classified as moderate by the researchers, and had suffered from the illness for several years. Over a one year period, the researchers asked the patients to complete assessments (including the HUI-3 questionnaire) after each acute exacerbation as well as once every three months.<sup>45</sup> During the study period, the HRQL for these patients averaged 0.79 or 0.76 (depending on the treatment). The mean value for both groups combined was approximately 0.78, when weighted by the number of participants in each group. We applied this estimate to all of the cases of chronic bronchitis by addressed our analysis.

For the course of cardiac disease following a nonfatal AMI, we relied on a study completed by Oostenbrink et al. (2001). This Dutch study traced about 2,650 patients after infrainguinal bypass surgery and compared the effects of different drug treatments. The mean length of follow-up was 21 months. These patients had an average age of 69 (compared to the average of 68 used in EPA’s analysis), and were likely to be somewhat more impaired than the average AMI survivor. The researchers administered the EQ-5D to determine the HRQL of the patients, and weighted the results using community values from a British study. For those patients experiencing an AMI, the subsequent HRQL averaged 0.58. We used this estimate for all of the post-AMI health states included in our assessment. While we considered instead using different estimates for cases with and without congestive heart failure or angina (as in the expert assignment and application of values from the chronic condition catalogue), we were unable to find an internally consistent set of weights that addressed all of the combinations of these conditions of interest.

<sup>45</sup> The domain and attribute descriptions used in the HUI-3 are provided in Appendix C.

It's important to note that other studies provide varying results. While the values from these other studies appear less suitable for transfer, they suggest that different approaches can yield a wide range of HRQL estimates. Brauer and Neumann (2005) report HRQL estimates for chronic bronchitis that range from 0.37 to 0.75 depending on the study approach, the disease severity, and the age of the patient. Estimates for different post-AMI health states also vary; for example, one study reports a value of 0.33 for the hospitalization period, angina studies report a range of 0.67 to 0.95, studies of congestive heart failure yield values ranging from 0.46 to 0.70, and (somewhat paradoxically) a study of angina and congestive heart failure combined yielded values ranging from 0.82 to 0.85 (higher than the value for heart failure alone from other studies). The reasons for this variation include the different populations studied, the different approaches to HRQL measurement used, and the different severities of illness considered. As discussed in Section 5.0 of this report, these varying estimates could be used to help quantify the uncertainty associated with estimating the HRQL impacts of these health conditions.

To estimate the QALY losses averted by the nonroad rule based on the values in Exhibit 15, we followed an approach that was very similar to the approach used to apply the values that resulted from the expert assignment and the EQ-5D MEPS catalogue analysis. However, because the studies provide weights from patient surveys rather than expert assignments, we assumed that they reflected all of the health-related factors affecting HRQL, not only those attributable to the condition. This raised two issues. First, average HRQL generally decreases with age, so that these estimates may reflect co-morbidities that would not be present in younger populations but would increase in older populations. Second, any decrement in HRQL calculated from these estimates may overstate the effect of the condition, because the estimates reflect aspects of the individuals' health that are not attributable to the condition.

To address these issues, we applied these condition weights as a proportionate reduction. For the comparison to average population HRQL, we first compared the study results for each condition to the estimate of average HRQL for an individual of the same age as the sample average (a 55 year old for chronic bronchitis and a 69 year old for AMI), using the data on population average health for the appropriate index (see Section 3.1.2). We then calculated the "with condition" HRQL as a percentage of the average HRQL for that age, and applied this percentage reduction to the HRQL estimates for all ages as relevant. These calculations are summarized in Exhibit 16.

<b>Exhibit 16</b>				
<b>HARVARD REGISTRY ESTIMATES CONVERTED TO DECREMENTS FROM AVERAGE HEALTH</b>				
<b>Condition (index)</b>	<b>Average Age</b>	<b>Population average HRQL</b>	<b>With condition HRQL</b>	<b>Percent reduction attributable to condition</b>
Chronic bronchitis (HUI-3)	55 years	0.84	0.78	6.7 percent
Nonfatal acute myocardial infarction (EQ-5D)	69 years	0.82	0.58	29.6 percent

Sources: See Exhibits 7 and 15.  
Notes: Values in exhibit are rounded results; unrounded estimates are used in actual calculations.

For the comparison to perfect health, we simply used the values as they were reported, i.e., the value of 0.78 for chronic bronchitis and of 0.58 for nonfatal AMI. These HRQL values are likely to be lower than the values associated solely with the condition of concern, since they are likely to include co-morbidities that are not directly related to chronic bronchitis or nonfatal AMI.

The two studies used in this assessment use different indices, raising questions about the appropriate index to use for preventable mortality. It was difficult to find a justification for using either the EQ-5D (consistent with the AMI study) or the HUI (consistent with the chronic bronchitis study), or for averaging the results under each index. (As illustrated earlier in Exhibit 7, the extent to which these indices yield different estimates of average population HRQL varies by age.) For simplicity and comparability, we apply the same EQ-5D estimates to assess preventable mortality for the Harvard Registry analysis as in the other two HRQL approaches used in this case study.

## SECTION 4.0: RESULTS OF CASE STUDY ANALYSIS

This section reports the results of the case study analysis based on our three approaches to HRQL assessment: the use of expert judgment to determine EQ-5D attributes, the application of weights from the EQ-5D MEPS catalogue for chronic conditions, and the transfer of values from selected studies in the Harvard Registry. We first report the results of the expert assignment, including both the attribute values selected to describe the effects of each health endpoint and the resulting estimates of HRQL with each illness. Similar results for the other two approaches (the EQ-5D catalogue weights and values from the Harvard Registry) were taken from completed analyses rather than calculated as part of this case study (see Exhibits 13 through 16), however, we adjust these results in our comparisons to average and perfect health. These comparisons are also illustrated below.

We then report our estimates of QALYs lost per case under each approach, including the losses associated with both nonfatal and fatal conditions. These results are presented undiscounted, and discounted using three and seven percent rates, consistent with current guidance for regulatory analysis (OMB 2003).<sup>46</sup> Our base case analysis compares the “with condition” results to average population HRQL at each age; in sensitivity analysis, we instead compare the “with condition” results to perfect health (i.e., a value of 1.0).

After calculating the per case QALY losses, we multiply the results by the number of cases averted by EPA’s nonroad rule to estimate the total QALY losses prevented by the rule. We then calculate the cost-effectiveness of the final rule under each HRQL approach. Throughout this section, we focus on our best estimates under each scenario; as noted in the introduction, this case study does not include the assessment of uncertainty required for regulatory analysis.

### 4.1 “With Condition” HRQL

In this section, we first report the results of the expert assignment, following the approach discussed in Section 3.2. We then discuss the adjustments made to the “with condition” HRQL estimates from all three approaches in the comparisons to average population health and to perfect health.

Under the expert assignment, we asked clinical experts to determine the EQ-5D attribute descriptions that best match the likely impacts of each of the nonfatal health endpoints assessed in this case study. These assessments address only the nonfatal endpoints; the “with condition” weighted value for fatal endpoints is zero under all of the approaches. In Exhibit 17, we summarize the attributes identified by the experts under the EQ-5D for each endpoint of concern.

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<sup>46</sup> As discussed in OMB 2003 (pp. 31-36), these discount rates reflect different assumptions regarding the appropriate comparison of impacts that occur in different time periods. The three percent rate represents the social rate of time preference (sometimes referred to as the consumption rate) while the seven percent rate represents the average pre-tax return to private investment. See OMB 2003 for more information on the assumptions underlying these rates as well on as the rationale for applying these rates to health-related benefits associated with regulatory interventions.

For each domain, we provide the median attribute score, as well as the maximum and minimum score reported by the experts.<sup>47</sup> As indicated in Exhibit 11, six respiratory experts assessed the chronic bronchitis endpoints, and five cardiovascular experts assessed the AMI-related endpoints. The definitions of the attributes corresponding to each score can be found in Appendix C, Exhibit C-1.

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<sup>47</sup> Due to the small number of experts involved, we use the median rather than the mean as our estimate of central tendency.

<b>Exhibit 17</b>						
<b>EXPERT ASSIGNMENT OF EQ-5D ATTRIBUTES FOR NONFATAL ENDPOINTS (median (min, max))</b>						
<b>Endpoint</b>	<b>Domain Attributes</b>					
	<b>Mobility</b>	<b>Self-Care</b>	<b>Usual Activities</b>	<b>Pain/Discomfort</b>	<b>Anxiety/Depression</b>	
<b><i>Chronic bronchitis:</i></b>						
Mild	1.0 (1,1)	1.0 (1,1)	1.0 (1,2)	1.0 (1,1)	1.0 (1,2)	
Moderate	2.0 (2,2)	2.0 (1,2)	2.0 (2,2)	2.0 (1,2)	2.0 (2,3)	
Severe	2.0 (2,3)	2.0 (2,3)	2.0 (3,3)	2.0 (1,3)	2.5 (2,3)	
<b><i>Acute myocardial infarction:</i></b>						
Hospitalization period	age < 65	3.0 (1,3)	2.0 (1,3)	3.0 (1,3)	2.0 (1,3)	3.0 (2,3)
	age ≥ 65	3.0 (1,3)	2.0 (1,3)	3.0 (2,3)	2.0 (1,3)	2.0 (2,3)
Class I angina only	age < 65	1.0 (1,1)	1.0 (1,1)	1.0 (1,2)	1.0 (1,1)	1.0 (1,2)
	age ≥ 65	1.0 (1,1)	1.0 (1,1)	1.0 (1,1)	1.0 (1,1)	1.0 (1,2)
Class II angina only	age < 65	2.0 (1,2)	1.0 (1,2)	2.0 (1,3)	2.0 (1,2)	2.0 (2,2)
	age ≥ 65	2.0 (1,2)	1.0 (1,2)	2.0 (1,2)	2.0 (1,2)	2.0 (1,2)
Class I congestive heart failure only	age < 65	1.0 (1,1)	1.0 (1,1)	1.0 (1,2)	1.0 (1,1)	1.0 (1,2)
	age ≥ 65	1.0 (1,1)	1.0 (1,1)	1.0 (1,2)	1.0 (1,1)	1.0 (1,2)
Class II congestive heart failure only	age < 65	2.0 (1,2)	1.0 (1,2)	2.0 (1,1)	2.0 (1,2)	2.0 (2,2)
	age ≥ 65	2.0 (1,2)	1.0 (1,2)	2.0 (1,2)	2.0 (1,2)	2.0 (1,2)
Class III congestive heart failure only	age < 65	2.0 (2,2)	2.0 (1,2)	2.0 (2,2)	2.0 (1,2)	2.0 (2,3)
	age ≥ 65	2.0 (2,2)	2.0 (1,2)	2.0 (2,3)	2.0 (1,2)	2.0 (2,2)
Class IV congestive heart failure only	age < 65	3.0 (3,3)	2.0 (2,3)	3.0 (3,3)	3.0 (1,3)	3.0 (2,3)
	age ≥ 65	3.0 (3,3)	3.0 (2,3)	3.0 (3,3)	3.0 (1,3)	3.0 (2,3)
Class I congestive heart failure with mild or moderate angina	age < 65	2.0 (1,2)	1.0 (1,1)	2.0 (1,3)	2.0 (1,2)	2.0 (1,2)
	age ≥ 65	2.0 (1,2)	1.0 (1,1)	2.0 (1,2)	2.0 (1,2)	1.0 (1,2)
Class II congestive heart failure with mild or moderate angina	age < 65	2.0 (1,2)	1.0 (1,2)	2.0 (1,2)	2.0 (1,3)	2.0 (2,2)
	age ≥ 65	2.0 (1,2)	1.0 (1,2)	2.0 (1,3)	2.0 (1,2)	2.0 (2,2)
Class III congestive heart failure with mild or moderate angina	age < 65	2.0 (2,2)	2.0 (1,2)	3.0 (2,2)	2.0 (2,2)	2.0 (2,3)
	age ≥ 65	2.0 (2,3)	2.0 (1,2)	3.0 (2,3)	2.0 (2,2)	2.0 (2,2)
Class IV congestive heart failure with mild or moderate angina	age < 65	3.0 (3,3)	3.0 (2,3)	3.0 (3,3)	3.0 (2,3)	3.0 (2,3)
	age ≥ 65	3.0 (3,3)	3.0 (2,3)	3.0 (3,3)	3.0 (2,3)	3.0 (2,3)
Notes: See Exhibits 9 and 10 for more detailed disease descriptions. Attributes corresponding to above scores are listed in Appendix C, Exhibit C-1.						

The EQ-5D allows a choice of three attribute levels within each domain, with lower numerical scores indicating fewer problems. An attribute associated with a score of “1” generally indicates no problems in that domain, a score of “2” generally indicates moderate problems, and a “3” generally indicates extreme problems. As shown by the median scores in the exhibit, in most cases the experts assigned scores that reflect the same or increasing problems to cases of increasing severity. Higher NYHA classes (indicating worsening conditions) generally received equal or higher scores. Scores for the older (above 65) age group are usually equal to or higher than the scores for the younger age group. However, the inverse is true for anxiety and depression. Based on our interviews with the experts (see Section 5.1), it appears that this inversion reflects the fact that a younger person might suffer more anxiety or depression regarding the impact of a serious illness on work and family.

In general, the range between the minimum and maximum scores suggests that the experts chose among adjacent descriptions (e.g., between a 1 and 2 or a 2 and 3). For some scenarios, the range reflects the full selection of values; i.e., different experts chose an attribute description corresponding to a 1, 2, or 3 to describe the effects of the same condition within a given domain. In other words, there was disagreement among the experts about whether the condition imposed no, moderate, or severe problems in the EQ-5D domain of concern. Because this exercise was intended primarily as a learning experience for the Committee members and completed with limited time and resources, we did not work with the experts to determine the rationale behind the variation in these scores.

The following exhibit summarizes the HRQL estimates for each nonfatal endpoint assessed, reporting the mean and median values that result from calculating HRQL based on the scores provided by each individual expert. (We provide the mean results for comparison, but use the median as our best estimate in the analysis that follows because of the small number of experts involved.) These estimates reflect the attribute scores weighted to reflect community preferences, on a scale where 1.0 corresponds to perfect health and zero corresponds to death. As discussed in Section 3.1.2 and 3.2.3, we assume that these estimates implicitly reflect comparison to perfect health; the effect of instead comparing to average age-adjusted health is discussed later in this section.

<b>Exhibit 18</b>			
<b>WITH CONDITION HRQL BASED ON EXPERT ASSIGNMENT OF EQ-5D ATTRIBUTES</b>			
<b>Endpoint</b>		<b>Median HRQL</b>	<b>Mean HRQL</b>
<b><i>Chronic bronchitis:</i></b>			
Mild		1.000	0.951
Moderate		0.597	0.608
Severe		0.385	0.298
<b><i>Acute myocardial infarction:</i></b>			
Hospitalization period	age < 65	0.283	0.225
	age ≥ 65	0.216	0.268
Class I angina only	age < 65	1.000	0.935
	age ≥ 65	1.000	0.969
Class II angina only	age < 65	0.708	0.731
	age ≥ 65	0.761	0.745
Class I congestive heart failure only	age < 65	1.000	0.935
	age ≥ 65	1.000	0.969
Class II congestive heart failure only	age < 65	0.761	0.749
	age ≥ 65	0.761	0.732
Class III congestive heart failure only	age < 65	0.597	0.574
	age ≥ 65	0.597	0.627
Class IV congestive heart failure only	age < 65	0.049	0.023
	age ≥ 65	0.030	0.028
Class I congestive heart failure with mild or moderate angina	age < 65	0.768	0.802
	age ≥ 65	0.816	0.826
Class II congestive heart failure with mild or moderate angina	age < 65	0.708	0.685
	age ≥ 65	0.708	0.699
Class III congestive heart failure with mild or moderate angina	age < 65	0.527	0.520
	age ≥ 65	0.527	0.453
Class IV congestive heart failure with mild or moderate angina	age < 65	0.030	(0.004)
	age ≥ 65	0.030	0.015
<p>Notes:            See Exhibits 9 and 10 for more detailed disease descriptions.            Median results are used in subsequent calculations; mean results are presented for comparison.            Reflects application of standard EQ-5D U.S. community weights to attribute scores reported by each expert.            Values reflect quality of life with the injury; not the decrement from normal health.            For fatal cases, “with injury” quality of life is zero.            Values in parenthesis are negative, reflecting the weighted value of attributes assessed at their lowest levels (e.g., “severe” limitations).</p>			

As indicated by the exhibit, the expert assignment suggests that these health conditions vary substantially in their impact on HRQL as measured by the EQ-5D. Some, such as mild chronic bronchitis and Class I angina or congestive heart failure, result in a negligible HRQL decrement; i.e., a median value of 1.0. This decrement increases as the conditions worsen. The most severe condition, Class IV congestive heart failure, leads to HRQL values close to zero, with median estimates of 0.05 or less. In general, the median values are identical for the above and below age 65 groups. However, in a few cases it appears that the impact is worse for the younger group (Class II angina only and Class I congestive heart failure with mild or moderate angina).<sup>48</sup> The relationship between the mean and median estimates varies depending on the extent to which the experts' scores clustered around a particular set of attribute values for each health endpoint.

For the remaining two approaches, we relied on research completed by others to assess the effects of the health conditions on HRQL. The values we use are presented in Exhibits 14 and 15 above. We then adjusted these estimates (as well as the expert assignment results) to allow comparison to both average and perfect health. The rationale behind these adjustments, described in detail in Section 3.0, can be summarized as follows.

- C In assessing the impacts of the health states, it appears that the experts largely focused on the condition of concern; i.e., did not take into account unrelated co-morbidities (see discussion in Sections 3.2 and 5.1). This approach implies a comparison that is more consistent with a perfect health scenario than with an average health scenario; comparison to average health would require consideration of age-related co-morbidities. Thus we used the unadjusted expert results (from Exhibit 18) in our comparisons to perfect health. For comparison to average age-adjusted health, we assumed that the condition would lead to the same proportionate reduction in HRQL.
- C Sullivan et al. (2005) calculated the EQ-5D catalogue values as decrements from median health. We subtracted these decrements from the estimates of average population health to determine the “with condition” HRQL. As discussed in Section 3.3, in the comparison to perfect health we held this “with condition” value constant, but added the difference between average and perfect health at each age to our estimate of the decrement. Thus the decrement increases with age under the perfect health scenario.
- C The values transferred from the two Harvard Registry studies are based on patient self-assessments and are likely to reflect overall HRQL, not solely the impact of the condition of concern, as discussed in Section 3.4. We compared these values to the estimates of average health for individuals of the mean age of each study sample to determine the proportionate decrement, then applied this proportion to average health at each age to determine the “with condition” values. For perfect health, we use the reported values,

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<sup>48</sup> The pattern in these results is not identical to the pattern in the median attribute values, because we calculate HRQL based on each individual expert's assessment before determining the mean or median. In other words, these HRQL values are not derived directly from the median attribute scores reported in Exhibit 15.

recognizing that this approach may lead us to overstate the extent to which the condition reduces HRQL under this scenario.

While these adjustments to the available values seem relatively sensible within the context of each individual HRQL approach (as described in more detail earlier), it leads to inconsistencies across the approaches in terms of the relationship of the “with condition” values to average and perfect health. Exhibit 19 provides examples of these relationships, focusing on the “with condition” values at the average age of incidence for each condition.

Exhibit 19									
COMPARISON OF HRQL RESULTS AT YEAR OF INCIDENCE									
Endpoint	Average Age at Incidence	Average Health Comparison				Perfect Health Comparison			
		Without Condition <sup>a</sup>	With Condition			Without Condition	With Condition		
			Expert Assignment <sup>b</sup>	EQ-5D Catalogue <sup>c</sup>	Harvard Registry <sup>d</sup>		Expert Assignment <sup>b</sup>	EQ-5D Catalogue <sup>c</sup>	Harvard Registry <sup>d</sup>
Chronic bronchitis	49	0.88	0.34 - 0.88	0.81	0.82	1.00	0.39-1.00	0.81	0.78
Acute myocardial infarction	53	0.85	0.03 - 0.85	0.70 - 0.81	0.60	1.00	0.03 - 1.00	0.70 - 0.81	0.58
	78	0.78	0.02 - 0.78	0.63 - 0.74	0.55	1.00	0.03 - 1.00	0.63 - 0.74	0.58
Preventable mortality - adults	74	0.78	0.00			1.00	0.00		
Preventable mortality - infants	0	1.00	0.00			1.00	0.00		

Notes:  
 Ranges reflect the results for the different health state subcategories assessed for the endpoint.  
 a. Without condition values for average health are based on the EQ-5D, except for the values for chronic bronchitis under the Harvard Registry approach, which are based on the HUI-3. At age 49, the HUI-3 value for average population health is 0.880, and the EQ-5D value is 0.875.  
 b. For the expert assignment, “with condition” health is assumed to be the same fraction of average health as of perfect health for all years of age affected.  
 c. For the EQ-5D catalogue, numerical decrements from average health are assumed to be constant across all years of age, and the difference between “without condition” average and perfect health is added to this decrement for the perfect health comparison.  
 d. For the Harvard Registry studies, “with condition” health is assumed to be a constant fraction of “without condition” health, this fraction is calculated based on the average age of the samples used in each study.

As illustrated by the exhibit, for the expert assignment the “with condition” values (and the decrement from normal health) are consistently lower under the average health scenario than under the perfect health scenario, because we apply the same percentage reduction to a lower value (average “without condition” HRQL is less than perfect HRQL). For the EQ-5D MEPS catalogue, the “with condition” values are the same under both scenarios, but the decrement is larger under the perfect health scenario and increases with age (because the difference between average and perfect health grows with age). For the Harvard Registry studies, which scenario results in larger values depends on age, because the percentage reduction from average population health is anchored at the average age of the underlying samples. The average for the Torrance et al. (1999) chronic bronchitis sample is 55 years, slightly higher than the average age at incidence used in our analysis. For the AMI study (Oostenbrink et al., 2001), the average age of the study sample is 69.

## **4.2 QALYs Lost per Case**

The next steps in the analysis involved comparing HRQL with each condition to HRQL absent the condition and calculating the decrement. This decrement was then multiplied by the duration of the condition (taking life expectancy into account) to estimate the associated QALY losses. In this section, we provide these estimates on a per case basis for each of the three HRQL approaches.

Exhibit 20 provides the results from the expert assignment in comparison to average age-adjusted population health, based on the approach described in Sections 3.1 and 3.2.

Exhibit 20				
EXPERT ASSIGNMENT OF EQ -5D ATTRIBUTES: QALY LOSSES PER CASE COMPARED TO AVERAGE HEALTH				
Endpoint	Discount Rate			
	Undiscounted	3 percent	7 percent	
<i>Chronic bronchitis</i>				
Mild	0.000	0.000	0.000	
Moderate	10.872	6.524	4.002	
Severe	16.589	9.954	6.107	
<i>Acute myocardial infarction</i>				
Hospitalization period	age < 65	0.009	0.009	0.009
	age ≥ 65	0.009	0.009	0.009
Class I angina only	age < 65	0.000	0.000	0.000
	age ≥ 65	0.000	0.000	0.000
Class II angina only	age < 65	6.148	3.981	2.594
	age ≥ 65	1.735	1.371	1.061
Class I congestive heart failure only	age < 65	0.000	0.000	0.000
	age ≥ 65	0.000	0.000	0.000
Class II congestive heart failure only	age < 65	0.810	0.753	0.686
	age ≥ 65	0.374	0.358	0.338
Class III congestive heart failure only	age < 65	1.367	1.271	1.158
	age ≥ 65	0.631	0.604	0.571
Class IV congestive heart failure only	age < 65	3.227	2.999	2.733
	age ≥ 65	1.520	1.455	1.374
Class I congestive heart failure with mild or moderate angina	age < 65	0.789	0.733	0.668
	age ≥ 65	0.288	0.276	0.260
Class II congestive heart failure with mild or moderate angina	age < 65	0.992	0.922	0.840
	age ≥ 65	0.458	0.438	0.414
Class III congestive heart failure with mild or moderate angina	age < 65	1.607	1.493	1.361
	age ≥ 65	0.742	0.710	0.671
Class IV congestive heart failure with mild or moderate angina	age < 65	3.293	3.060	2.788
	age ≥ 65	1.520	1.455	1.374
<i>Preventable mortality</i>				
Infants	70.246	27.431	13.520	
Adults, no lag	10.874	8.088	5.912	
Adults, one year lag	10.874	7.853	5.525	
Adults, two year lag	10.874	7.624	5.163	
Adults, three year lag	10.874	7.402	4.826	
Adults, four year lag	10.874	7.186	4.510	

The exhibit illustrates the combined effects of the HRQL impacts from Exhibit 18 and the assumptions regarding age at incidence, duration, and life expectancy summarized earlier in

Exhibit 6. Not surprisingly, in cases where the results from the experts indicated that the conditions were not likely to lead to noticeable problems under any of the domains assessed under the EQ-5D, the QALY losses are zero. The losses increase as both the HRQL decrement and duration of the condition increase. The effect of the increasing decrements in HRQL is most apparent in the results for chronic bronchitis, where we assume that all cases have the same duration, beginning at age 49 and continuing throughout the remaining life span. For these cases, the QALY losses increase as the severity of the condition increases.

Interpreting the results for the cardiac endpoints is more complex. As discussed in Section 3.1.1, we do not count the years of preventable mortality in the assessment of the nonfatal cardiac endpoints because this mortality is presumably captured in the separate estimates of fatal cases. For the cardiac conditions, the duration (or period of time an individual survives with the illness) is relatively short, particularly for persons with congestive heart failure. In these cases, the HRQL losses are high but the duration of the condition (i.e., the remaining life span with the disease) is low, leading to comparatively small QALY losses.

For fatal cases, HRQL drops to zero and is compared to average HRQL for each year of age for the remaining life span, using U.S. population estimates of average mortality rates by year of age. The impact per case is much greater for infants than adults because of the substantially longer remaining life span. The time lag noted in the exhibit reflects EPA's assumptions regarding the delay between the decrease in exposure and the decrease in mortality, and is reflected in the discounting.

Overall, the discount rates have the expected impact, with higher discount rates leading to smaller present values. Discounting does not noticeably affect the values for hospitalization because these effects occur in the first year and are of short duration (5.5 days). Larger differences occur for the long term impacts, because the lower rate increases the contribution of future year HRQL decrements to the total present value by discounting them by a smaller amount.

We also compare the HRQL with each condition to perfect health (a value of 1.0) in sensitivity analysis. Exhibit 21 provides the results from the expert assignment using this comparison.

<b>Exhibit 21</b>				
<b>EXPERT ASSIGNMENT OF EQ -5D ATTRIBUTES: QALY LOSSES PER CASE COMPARED TO PERFECT HEALTH</b>				
<b>Endpoint</b>		<b>Discount Rate</b>		
		<b>Undiscounted</b>	<b>3 percent</b>	<b>7 percent</b>
<b><i>Chronic bronchitis</i></b>				
Mild		0.000	0.000	0.000
Moderate		13.477	7.943	4.799
Severe		20.563	12.120	7.322
<b><i>Acute myocardial infarction</i></b>				
Hospitalization period	age < 65	0.011	0.010	0.010
	age ≥ 65	0.012	0.011	0.011
Class I angina only	age < 65	0.000	0.000	0.000
	age ≥ 65	0.000	0.000	0.000
Class II angina only	age < 65	3.134	4.872	7.634
	age ≥ 65	1.406	1.823	2.313
Class I congestive heart failure only	age < 65	0.000	0.000	0.000
	age ≥ 65	0.000	0.000	0.000
Class II congestive heart failure only	age < 65	0.955	0.887	0.808
	age ≥ 65	0.477	0.457	0.432
Class III congestive heart failure only	age < 65	1.611	1.497	1.364
	age ≥ 65	0.806	0.771	0.728
Class IV congestive heart failure only	age < 65	3.802	3.534	3.220
	age ≥ 65	1.940	1.856	1.754
Class I congestive heart failure with mild or moderate angina	age < 65	0.930	0.864	0.787
	age ≥ 65	0.367	0.352	0.332
Class II congestive heart failure with mild or moderate angina	age < 65	1.169	1.086	0.990
	age ≥ 65	0.585	0.559	0.528
Class III congestive heart failure with mild or moderate angina	age < 65	1.893	1.759	1.603
	age ≥ 65	0.947	0.906	0.856
Class IV congestive heart failure with mild or moderate angina	age < 65	3.880	3.606	3.286
	age ≥ 65	1.940	1.856	1.754
<b><i>Preventable mortality</i></b>				
Infants		79.529	29.436	14.006
Adults, no lag		14.362	10.627	7.721
Adults, one year lag		14.362	10.317	7.216
Adults, two year lag		14.362	10.017	6.744
Adults, three year lag		14.362	9.725	6.303
Adults, four year lag		14.362	9.442	5.891

This exhibit shows similar patterns than those discussed under Exhibit 20. However, the comparison to perfect health increases the difference between the with and without condition values, leading to larger estimates of QALY losses.

The second HRQL approach involves the application of preliminary EQ-5D values from the MEPS catalogue of chronic conditions developed by Sullivan et al. (2005), as discussed in Section 3.3. The health conditions were broken into fewer subcategories for this assessment. As indicated in the exhibit below, we use a single category for chronic bronchitis rather than separating out different severity levels. For the post-AMI scenarios, we use different decrements for each combination of health states (i.e., for the AMI itself, and for angina and congestive heart failure, from Exhibit 14). The decrements for each condition do not vary by age group; however, for the AMI related conditions, our assumptions for average age at incidence and remaining life expectancy vary for the above and below 65 groups. For preventable mortality, we use the same approach (and the same EQ-5D values) as for the expert assignment. The resulting estimates of QALY losses in comparison to average age-adjusted health are presented in Exhibit 22 below; the approach used in this assessment is described in Sections 3.1 and 3.3 above.

<b>Exhibit 22</b>				
<b>EQ-5D MEPS CATALOGUE OF CHRONIC CONDITIONS: QALY LOSSES PER CASE COMPARED TO AVERAGE HEALTH</b>				
<b>Endpoint</b>		<b>Discount Rate</b>		
		<b>Undiscounted</b>	<b>3 percent</b>	<b>7 percent</b>
<i>Chronic bronchitis</i>		2.128	1.274	0.775
<i>Acute myocardial infarction</i>				
Hospitalization period	age < 65	0.001	0.001	0.001
	age ≥ 65	0.001	0.001	0.001
Angina only	age < 65	2.001	1.277	0.821
	age ≥ 65	0.742	0.585	0.451
Congestive heart failure only	age < 65	0.439	0.408	0.372
	age ≥ 65	0.220	0.210	0.199
Congestive heart failure and angina	age < 65	0.586	0.544	0.496
	age ≥ 65	0.293	0.280	0.265
No angina or congestive heart failure	age < 65	1.047	0.668	0.430
	age ≥ 65	0.388	0.306	0.236
<i>Preventable mortality</i>				
Infants		70.246	27.431	13.520
Adults, no lag		10.874	8.088	5.912
Adults, one year lag		10.874	7.853	5.525
Adults, two year lag		10.874	7.624	5.163
Adults, three year lag		10.874	7.402	4.826
Adults, four year lag		10.874	7.186	4.510

This exhibit illustrates the combined effects of the HRQL impacts from Exhibit 14 and the assumptions regarding age at incidence, duration, and life expectancy summarized earlier in Exhibit 6. For chronic bronchitis, the QALY losses are roughly equal to only about 20 percent of the estimates for moderately severe cases from the expert assignment. Because we use the same duration assumptions in both cases, this difference is attributable entirely to the smaller decrement estimated in the preliminary estimates from the EQ-5D MEPS catalogue.

For the cardiac endpoints, the HRQL impacts increase as the condition becomes more severe, but the QALY losses do not follow the same pattern due to the duration assumptions. As illustrated in Exhibit 14, AMI alone leads to the smallest HRQL decrement, adding angina roughly doubles the decrement, and adding congestive heart failure leads to the largest decrement. However, the duration assumptions make it appear that congestive heart failure has a smaller impact in terms of QALY losses. As noted earlier, to avoid double-counting with the estimates of preventable mortality, we only assess post-AMI HRQL for survivors for their remaining life span, which is quite short for those cases involving congestive heart failure; two years for the over 65 age group and four years for the under 65 age group.

In comparison to the QALY losses estimated through the expert assignment process, the results for angina only from the EQ-5D catalogue are between those estimated for Class I and Class II angina. The EQ-5D congestive heart failure results are also between the expert results for Classes I and II without angina, and smaller than those for the more severe classes. For congestive heart failure and angina, the EQ-5D catalogue generally results in lower QALY estimates than the expert assignment. However, we did not ask the experts to assess the HRQL for AMI survivors without angina or congestive heart failure and instead assume that these individuals will return to normal health (i.e., average age-adjusted HRQL under our base case scenario). In contrast, the EQ-5D catalogue results suggest that such survivors will in fact experience a reduced HRQL.

For fatal cases, the QALY losses are identical to the estimates used in the expert assignment, since we rely on the same data on duration and age-adjusted population average HRQL in both cases. The discount rates have the expected impact, leading to smaller present values as the discount rate increases.

We also compare the HRQL with each condition to perfect health (a value of 1.0) in sensitivity analysis. Exhibit 23 provides the results from the EQ-5D catalogue using this comparison. While this exhibit shows similar patterns as those discussed under Exhibit 22, the comparison to perfect health again increases the difference between the with and without condition values, leading to larger estimates of QALY losses.

<b>Exhibit 23</b>				
<b>EQ-5D MEPS CATALOGUE OF CHRONIC CONDITIONS: QALY LOSSES PER CASE COMPARED TO PERFECT HEALTH</b>				
<b>Endpoint</b>		<b>Discount Rate</b>		
		<b>Undiscounted</b>	<b>3 percent</b>	<b>7 percent</b>
<i>Chronic bronchitis</i>		8.374	4.751	2.745
<i>Acute myocardial infarction</i>				
Hospitalization period	age < 65	0.003	0.003	0.003
	age ≥ 65	0.001	0.001	0.001
Angina only	age < 65	7.087	4.325	2.669
	age ≥ 65	3.165	2.478	1.895
Congestive heart failure only	age < 65	1.045	0.971	0.885
	age ≥ 65	0.652	0.624	0.590
Congestive heart failure and angina	age < 65	1.191	1.107	1.008
	age ≥ 65	0.725	0.694	0.656
No angina or congestive heart failure	age < 65	6.133	3.716	2.277
	age ≥ 65	2.811	2.199	1.680
<i>Preventable mortality</i>				
Infants		79.529	29.436	14.006
Adults, no lag		14.362	10.627	7.721
Adults, one year lag		14.362	10.317	7.216
Adults, two year lag		14.362	10.017	6.744
Adults, three year lag		14.362	9.725	6.303
Adults, four year lag		14.362	9.442	5.891

The final HRQL approach involves the application of values from selected studies from the Harvard Registry. This assessment applies two HRQL values, one for all cases of chronic bronchitis (from Torrance et al., 1999) and one for all post-AMI categories (from Oostenbrink et al., 2001). However, we again calculate duration and life expectancy separately for the above and below age 65 groups for cases including or excluding congestive heart failure, to increase the comparability to the results under the other HRQL approaches. For preventable mortality, we use the same approach and EQ-5D values as elsewhere. The resulting estimates of QALY losses in comparison to average age-adjusted health are presented in Exhibit 24 below; the approach used in this assessment is described in Sections 3.1 and 3.4 above.

<b>Exhibit 24</b>				
<b>TRANSFER OF VALUES FROM HARVARD REGISTRY STUDIES: QALY LOSSES PER CASE COMPARED TO AVERAGE HEALTH</b>				
<b>Endpoint</b>		<b>Discount Rate</b>		
		<b>Undiscounted</b>	<b>3 percent</b>	<b>7 percent</b>
<i>Chronic bronchitis</i>		1.789	1.076	0.661
<i>Acute myocardial infarction</i>				
Without congestive heart failure	age < 65	6.236	4.038	2.632
	age ≥ 65	1.346	1.014	0.748
With congestive heart failure	age < 65	1.006	0.935	0.852
	age ≥ 65	0.465	0.445	0.420
<i>Preventable mortality</i>				
Infants		70.246	27.431	13.520
Adults, no lag		10.874	8.088	5.912
Adults, one year lag		10.874	7.853	5.525
Adults, two year lag		10.874	7.624	5.163
Adults, three year lag		10.874	7.402	4.826
Adults, four year lag		10.874	7.186	4.510

This exhibit illustrates the combined effects of the HRQL impacts from Exhibit 15 and the assumptions regarding age at incidence, duration, and life expectancy summarized earlier in Exhibit 6. For chronic bronchitis, a single value is used to assess the QALY losses for all cases. While the HRQL estimate for chronic bronchitis is smaller than the single estimate for the post-AMI disease state, some of the post-AMI conditions result in smaller estimates of QALY losses. This occurs because of the shorter duration of the effects of morbidity prior to mortality; as noted earlier, cardiac conditions can dramatically decrease life expectancy. Again, preventable mortality is not included in the post-AMI estimates to avoid double counting with the estimates of fatal cases. For the fatal cases, the QALY losses are identical to the estimates used in the other assessments and rely on the same data. As before, the discount rates have the expected impact, leading to smaller present values as the discount rate increases.

We also compare HRQL with each condition to perfect health (a value of 1.0) in sensitivity analysis. Exhibit 25 provides the results from the Harvard Registry studies using this comparison. While this exhibit shows similar patterns than those discussed under Exhibit 24, the comparison to perfect health again increases the difference between the with and without condition values, leading to larger estimates of QALY losses for all conditions.

<b>Exhibit 25</b>				
<b>TRANSFER OF VALUES FROM HARVARD REGISTRY STUDIES: QALY LOSSES PER CASE COMPARED TO PERFECT HEALTH</b>				
<b>Endpoint</b>		<b>Discount Rate</b>		
		<b>Undiscounted</b>	<b>3 percent</b>	<b>7 percent</b>
<i>Chronic bronchitis</i>		7.360	4.338	2.621
<i>Acute myocardial infarction</i>				
Without congestive heart failure	age < 65	10.971	7.002	4.504
	age ≥ 65	2.551	1.917	1.407
With congestive heart failure	age < 65	1.680	1.561	1.423
	age ≥ 65	0.840	0.804	0.759
<i>Preventable mortality</i>				
Infants		79.529	29.436	14.006
Adults, no lag		14.362	10.627	7.721
Adults, one year lag		14.362	10.317	7.216
Adults, two year lag		14.362	10.017	6.744
Adults, three year lag		14.362	9.725	6.303
Adults, four year lag		14.362	9.442	5.891
Notes:				
See Sections 3.1 and 3.4 for detailed information on health conditions, assumptions, and calculations.				
The AMI scenarios differ only in the age and life expectancy assumptions applied, the same HRQL decrement is applied in both scenarios and for both age groups.				

## 4.2 Total QALY Losses

To determine the total QALY losses attributable to the regulations, we multiply the per-case losses by the number of cases for each condition. The losses per case are provided in Exhibits 18 through 25 above; the estimates of cases avoided are based on Exhibit 2 and subdivided using the percentages in Exhibits 9 and 10 where relevant. The results for each HRQL approach are reported in the exhibits below for the comparison to average health and perfect health respectively. These estimates represent the life time losses for all cases averted by a one year reduction in pollution levels as of the year 2030.

<b>Exhibit 26</b>			
<b>TOTAL QALY LOSSES IN COMPARISON TO AVERAGE HEALTH (2030)</b>			
<b>HRQL Approach</b>	<b>Undiscounted</b>	<b>3 Percent Discount Rate</b>	<b>7 Percent Discount Rate</b>
<i>Expert Assignment of EQ-5D Attributes</i>			
Nonfatal chronic bronchitis	27,072	16,245	9,966
Nonfatal AMI	13,683	10,259	7,823
Preventable mortality	132,037	92,852	63,605
Total	172,792	119,356	81,395
<i>EQ-5D MEPS Catalogue of Chronic Conditions</i>			
Nonfatal chronic bronchitis	11,915	7,136	4,341
Nonfatal AMI	12,367	8,848	6,402
Preventable mortality	132,037	92,852	63,605
Total	156,319	108,837	74,349
<i>Transfer from Selected Harvard Registry Studies</i>			
Nonfatal chronic bronchitis	10,017	6,028	3,699
Nonfatal AMI	21,798	15,246	10,782
Preventable mortality	132,037	92,852	63,605
Total	163,852	114,126	78,086

As indicated by the exhibit, the different approaches to estimating HRQL impacts lead to differing results. Because the estimates for preventable mortality are identical under all three approaches, these differences are driven by the approaches used to value the nonfatal endpoints. The expert assignment yields values for chronic bronchitis that are more than twice as large as the estimates from the EQ-5D catalogue or Harvard Registry studies. For the AMI endpoints, the Harvard Registry studies lead to estimates of QALY losses that are greater than the results under the expert assignment or the EQ-5D catalogue. The estimates of the number of cases avoided, age at incidence, and life expectancy are constant across all three approaches, hence these results reflect the differing estimates of the HRQL decrement associated with each condition.

Exhibit 27 provides the estimates of QALY losses that result when the “with condition” HRQL is compared to perfect health rather than to average age-adjusted HRQL. As noted earlier

and illustrated in Exhibit 19, which approach leads to the largest estimates of “with condition” HRQL varies across the comparisons to perfect and average health, due to the differing adjustments used in these comparisons. However, as expected, the results for each individual HRQL approach are larger than in the comparison to average HRQL; perfect health is represented by a constant value of 1.0 across all years of age, while average health declines with age as shown earlier in Exhibit 7. For example, when discounted at three percent, total QALY losses increase by about 25 percent under the perfect health scenario using the expert assignment results.

<b>Exhibit 27</b>			
<b>TOTAL QALY LOSSES IN COMPARISON TO PERFECT HEALTH (2030)</b>			
<b>HRQL Approach</b>	<b>Undiscounted</b>	<b>3 Percent Discount Rate</b>	<b>7 Percent Discount Rate</b>
<i>Expect Assignment of EQ-5D Attributes</i>			
Nonfatal chronic bronchitis	33,557	19,779	11,948
Nonfatal AMI	17,222	12,819	9,722
Preventable mortality	174,093	121,848	82,996
Total	224,872	154,447	104,666
<i>EQ-5D MEPS Catalogue of Chronic Conditions</i>			
Nonfatal chronic bronchitis	46,892	26,605	15,373
Nonfatal AMI	55,277	38,332	26,923
Preventable mortality	174,093	121,848	82,996
Total	276,261	186,785	125,292
<i>Transfer from Selected Harvard Registry Studies</i>			
Nonfatal chronic bronchitis	41,218	24,295	14,676
Nonfatal AMI	38,975	27,017	18,966
Preventable mortality	174,093	121,848	82,996
Total	254,286	173,160	116,638

### 4.3 Cost-Effectiveness

To determine the cost-effectiveness of the nonroad regulations under the three HRQL approaches noted above, we first define the costs to be included in the ratio and then divide these costs by the QALY losses estimated in Exhibits 26 and 27. We also include the ratio of lives and life years saved to costs. These steps are discussed in more detail below.

#### 4.3.1 Adjustments to Regulatory Compliance Costs

Calculating the cost-effectiveness of the regulations; i.e., the cost per QALY, involves first reviewing the EPA cost estimate to ensure that it is consistent with recommended best practices for this type of analysis. As discussed in Section 2.1, EPA estimated that the nonroad regulations would cost \$2.0 billion annually as of 2030, when all engines in use are expected to meet the new standards.<sup>49</sup> There are two issues related to using this estimate in a QALY-based cost-effectiveness analysis: (1) how to address savings related to the use of health resources (i.e., medical costs and lost time) associated with the averted cases of illness included in the QALY measure, and (2) how to address those benefits that are quantified in the benefit-cost analysis but not addressed in the QALY estimates; i.e., the short-term health effects and visibility benefits listed earlier in Exhibit 2. As indicated by Exhibit 3, EPA also notes that a number of other potential benefits could not be quantified.

The current OMB guidance for regulatory cost-effectiveness analysis notes the following:

*“With regard to measuring costs, you should be sure to include all the relevant costs to society - whether public or private. Rulemakings may also yield cost savings (e.g., energy savings associated with new technologies). The numerator in the cost-effectiveness ratio should reflect net costs, defined as the gross cost incurred to comply with the requirements (sometimes called “total” costs) minus any cost savings. You should be careful to avoid double-counting effects in both the numerator and the denominator of the cost-effectiveness ratios. For example, it would be incorrect to reduce gross costs by an estimated monetary value on life extension if life-years are already used as the effectiveness measure in the denominator.”* (OMB 2003, pp. 11-12)

The EPA estimate of costs appears consistent with this definition; it includes the gross costs of regulatory compliance net of compliance-related cost-savings, and does not double-count impacts included in the benefits estimates.

However, EPA’s cost estimate does not address the health care-related savings associated with reducing the incidence of those health conditions represented by the QALY measures. The Panel on Cost-Effectiveness in Health and Medicine lists four types of costs that should be included in the numerator of the cost-effectiveness ratio: changes in the use of health care resources, changes in the use of non-health care resources, changes in the use of informal caregiver time, and changes in the use of patient time due to treatment (Gold et al., p. 177).

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<sup>49</sup> All cost estimates represent 2000 dollars unless otherwise noted.

For health care resource costs, EPA provided estimates of the medical costs associated with chronic bronchitis and nonfatal AMI in the Hubbell (2004) analysis we use to support this case study.

- C For chronic bronchitis beginning at age 49, EPA's analysis results in estimates of the lifetime medical costs per case of approximately \$23,240 (with a three percent discount rate) or \$17,205 (with a seven percent discount rate), based on Cropper and Krupnick (1990).<sup>50</sup> When multiplied by the 5,600 cases of chronic bronchitis averted annually by the rule, these medical costs total roughly 0.1 billion.<sup>51</sup>
- C For nonfatal AMIs, EPA estimates medical costs based on Wittels et al. (1990) and Russell et al. (1998) as a simple average of \$65,902 over five years (Hubbell (2004), p. 23 and EPA (2005), p. G-40).<sup>52</sup> If multiplied by the estimated 15,000 nonfatal AMIs averted by the regulations annually, these medical costs total roughly \$1.0 billion.

In combination, these EPA estimates suggest that the medical costs associated with the averted cases of chronic bronchitis and nonfatal AMI may total roughly \$1.1 billion. If we subtract these medical costs from the regulatory costs of \$2.0 billion, net costs total \$0.9 billion.

For time losses, the Panel notes that overall decreases in productivity associated with illness are most appropriately included in the QALY measure; only the time losses associated with the production of better health (i.e., with treatment and caregiving) should be included in the numerator (Gold et al. (1996), pp. 176-183). This recommendation appears consistent with the QALY measures used in this case study. Our estimates are based primarily on the EQ-5D, which includes the ability to work in the "usual activity" domain; the HUI also addresses a number of functional limitations that affect productivity.

The EPA analyses that we rely upon for this case study provide estimates of total lost earnings attributable to morbidity but do not provide separate estimates solely for the time spent in treatment and exclude caregiver losses.<sup>53</sup> Thus we lack the data needed to adjust regulatory costs to reflect avoided time losses in a manner that is consistent with the Panel's recommendations.

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<sup>50</sup> Calculated based on BenMAP data that indicates that medical costs represent roughly 24 percent of the sum of medical costs and lost earnings for chronic bronchitis (data provided by Jim Neumann to Lisa Robinson, May 3, 2005). The EPA documents only report the total value for medical costs and lost earnings combined (Hubbell (2004), p. 22 and EPA (2005), p. G-39).

<sup>51</sup> We round to the nearest 0.1 billion for consistency with EPA's presentation of regulatory costs. Otherwise, these estimates total \$130 million or \$96 million depending on whether a 3 or 7 percent discount rate is used.

<sup>52</sup> Hubbell notes that these two sources provide substantially different estimates and that he was unable to determine the cause of the differences or to determine how to appropriately discount the estimates (Hubbell (2004), p. 23 and EPA (2005), pp. G-39 to G-40).

<sup>53</sup> These estimates are calculated for chronic bronchitis and nonfatal AMI based on Cropper and Krupnick (1990) (EPA 2004, p. 9-156, Hubbell 2004, p. 22-23, and EPA 2005, pp. G-39 to G-41); EPA does not estimate lost earnings for preventable mortality.

The second issue related to the calculation of costs involves the treatment of benefits not included in the QALY measure. According to EPA’s analysis, the total value of the benefits not reflected in the QALY measure (i.e., benefits excluding preventable mortality, chronic bronchitis and nonfatal AMI) total about \$2.3 billion annually as of the year 2030 (see Exhibit 2). About 76 percent (\$1.7 billion) of this value is attributable to improved visibility, the remainder is attributable to averted acute or short-term health effects. In other words, the combined value of averting those short-term health impacts and environmental impacts not included in our QALY estimates exceeds the costs of the regulations. Thus netting these benefit values out of the regulatory costs leads to negative costs; i.e., to cost-savings. The resulting cost estimates are provided in Exhibit 28 below.

<b>Exhibit 28</b>	
<b>NET REGULATORY COSTS IN 2030</b>	
<b>(2000 dollars)</b>	
Regulatory Compliance Costs	\$2.0 billion
Medical Cost-Savings, Chronic Bronchitis	(\$0.1 billion)
Medical Cost-Savings, Nonfatal AMI	(\$1.0 billion)
Subtotal	\$0.9 billion
Benefit values not included in QALY estimates	(\$2.3 billion)
Total	(\$1.4 billion)
Notes: See text for derivation of estimates. Values in parentheses are negative, i.e., represent cost-savings.	

#### **4.3.2 Measures of Cost-Effectiveness**

In Exhibit 29, we divide the net regulatory costs from Exhibit 28 by the QALY estimates from Exhibit 26 to estimate the cost per QALY under the average health scenario. We apply two cost estimates; the first (costs of \$0.9 billion) reflects annual regulatory costs net of medical costs only, the second (savings of \$1.4 billion) reflects regulatory costs net of both medical costs and the value of benefits not addressed by the QALY measure. However, because the latter measure reflects savings, the resulting ratio is not interpretable and hence is not reported. All results are rounded to two significant figures.

<b>Exhibit 29</b>			
<b>COSTS PER QALY, COMPARED TO AVERAGE HEALTH (2030)</b>			
<b>HRQL Approach</b>	<b>Undiscounted</b>	<b>3 Percent Discount Rate</b>	<b>7 Percent Discount Rate</b>
<i>Expert Assignment of EQ-5D Attributes</i>			
Regulatory compliance costs, net of health treatment savings = \$0.9 billion	\$5,200	\$7,500	\$11,000
Regulatory compliance costs, net of health treatment savings and value of additional benefits = (\$1.4 billion)	cost-saving		
<i>EQ-5D MEPS Catalogue of Chronic Conditions</i>			
Regulatory compliance costs, net of health treatment savings = \$0.9 billion	\$5,800	\$8,300	\$12,000
Regulatory compliance costs, net of health treatment savings and value of additional benefits = (\$1.4 billion)	cost-saving		
<i>Transfer from Selected Harvard Registry Studies</i>			
Regulatory compliance costs, net of health treatment savings = \$0.9 billion	\$5,500	\$7,900	\$12,000
Regulatory compliance costs, net of health treatment savings and value of additional benefits = (\$1.4 billion)	cost-saving		

As indicated by the exhibit, each approach leads to somewhat similar estimates in terms of costs per QALY. When compared to regulatory costs net of medical costs, the undiscounted cost per QALY ranges from about \$5,200 to \$5,800. This cost per QALY increases as the discount rate increases, because the larger discount rate leads to smaller present value estimates for the QALYs included in the denominator. When costs are adjusted to net out both medical costs and the value of those quantified benefits not included in the QALY estimates, savings result.

In Exhibit 30, we divide net regulatory costs by the QALY estimates from Exhibit 27 to estimate the cost per QALY under the perfect health scenario. As expected, these estimates are

smaller, because the QALY estimates included in the denominator are larger under this scenario. Which approach leads to the largest estimates varies depending on whether the comparison is to average or perfect health, due to the adjustments that we make as part of these comparisons.

<b>Exhibit 30</b>			
<b>COSTS PER QALY, COMPARED TO PERFECT HEALTH (2030)</b>			
<b>HRQL Approach</b>	<b>Undiscounted</b>	<b>3 Percent Discount Rate</b>	<b>7 Percent Discount Rate</b>
<i>Expect Assignment of EQ-5D Attributes</i>			
Regulatory compliance costs, net of health treatment savings = \$0.9 billion	\$4,000	\$5,800	\$8,600
Regulatory compliance costs, net of health treatment savings and value of additional benefits = (\$1.4 billion)	cost-saving		
<i>EQ-5D MEPS Catalogue of Chronic Conditions</i>			
Regulatory compliance costs, net of health treatment savings = \$0.9 billion	\$3,300	\$4,800	\$7,200
Regulatory compliance costs, net of health treatment savings and value of additional benefits = (\$1.4 billion)	cost-saving		
<i>Transfer from Selected Harvard Registry Studies</i>			
Regulatory compliance costs, net of health treatment savings = \$0.9 billion	\$3,500	\$5,200	\$7,700
Regulatory compliance costs, net of health treatment savings and value of additional benefits = (\$1.4 billion)	cost-saving		

In Exhibit 31 below, we report two other ratios, the costs of compliance per preventable death avoided and per life year gained. In these cases, we do not net out the value of health care related savings from the estimates of regulatory compliance costs.

<b>Exhibit 31</b>			
<b>COSTS PER CASE OF PREVENTABLE MORTALITY AND PER LIFE YEAR GAINED (2030)</b>			
	<b>undiscounted</b>	<b>3 percent discount rate</b>	<b>7 percent discount rate</b>
<b>Averted deaths</b>	12,000 preventable deaths	12,000 preventable deaths	12,000 preventable deaths
<b>Averted life year losses</b>	130,000 years	93,000 years	64,000 years
<b>Regulatory compliance costs</b>	\$2.0 billion	\$2.0 billion	\$2.0 billion
<i>Compliance Cost per Preventable Fatality Averted</i>	\$170,000	\$170,000	\$170,000
<i>Compliance Cost per Life Year Gained</i>	\$15,000	\$22,000	\$31,000

Under these approaches, the costs per preventable fatality averted is the same regardless of the discount rate, while discounting leads to increases in the costs per life year gained.

## SECTION 5.0: LIMITATIONS

This case study was prepared as a learning exercise for the IOM Committee to Evaluate Measures of Health Benefits for Environmental, Health, and Safety Regulation, and as such lacks some of the detail and complexity that would be required in an actual regulatory analysis. Perhaps most importantly, current guidance (OMB 2003) requires substantial assessment of uncertainty, while this case study largely relies on mean or median estimates and includes only limited sensitivity analysis. The existing guidelines for regulatory analysis require that agencies provide both qualitatively and quantitative information on uncertainty. As of January, 2005, formal probabilistic analysis is required for all rules with impacts that exceed \$1 billion annually, which would include the nonroad rule that is the subject of this case study. The OMB guidance also emphasizes the importance of providing information on impacts that cannot be quantified or that can be quantified in physical terms but not assigned a value. The EPA analysis upon which this case study is based provides substantial discussion of uncertainty and nonquantified benefits, and includes quantitative assessment of the degree of uncertainty in both the cost and benefit estimates. In addition, the Committee did not assess the distribution of the effects of this regulation, which is also required under the OMB guidelines and other administrative and legal authorities. Again, EPA's analysis provides information on related topics.

In this section, we briefly discuss the sources of uncertainty most directly related to our application of the three HRQL approaches. We first discuss the comments received from the experts involved in the assignment of the EQ-5D attribute levels, and then discuss other key areas of uncertainty.

### 5.1 Comments from Experts Involved in EQ-5D Assignment

Between one and two weeks following receipt of the experts' assignments, we held scheduled phone interviews with all 11 clinicians who participated.<sup>54</sup> Six pulmonary or respiratory disease experts completed the assignments for chronic bronchitis and five cardiologists completed them for the post-AMI health states, as discussed in Section 3.2 of this case study.

In conversations lasting from 10 to 20 minutes, we first asked the clinicians open-ended questions, beginning with their overall impression of the task they were asked to complete, their mental model when characterizing a typical patient for a particular scenario (literally, what they had in mind as they answered the assessment questions), and whether they took into account the effects of possible co-morbidities or age-related impacts on HRQL or instead thought only about the condition described in the scenario. Other questions elicited their views on the domain attributes, the clarity of the instructions, and the ways in which the expert assignment process might be improved; we also asked them to estimate the time they spent on the assignments.

As discussed earlier, the single respiratory disease endpoint, chronic bronchitis, was described in three scenarios as "mild," "moderate," or "severe." The post-AMI health endpoints

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<sup>54</sup> Wilhelmine Miller conducted these interviews.

included 11 scenarios, and the experts were asked to consider patients younger than age 65 and 65 or older separately, so they had 22 separate sets of EQ-5D assignments to complete. The cardiovascular disease assignment also differed from the respiratory disease assignment in that we used the NYHA Classes I through IV for angina and congestive heart failure to characterize health states, rather than describing groups of symptoms.

All of the pulmonologists and cardiologists reported that they had in mind a typical patient with the condition, someone of average health for their age. At the same time, they uniformly assumed that they were assessing someone without additional co-morbidities. Several said this was because the scenarios did not specifically list additional co-morbidities. Many of the experts reported that their frame of reference was their own patients, “people who walk into my office every day,” and one said it was difficult to resist being influenced by the “last three or four patients with the condition that I saw.” One cardiologist suggested that the NYHA classes essentially “calibrates by age,” i.e., what is “limiting angina” for a 55-year-old would probably be a higher level of functioning if measured objectively (pain on running up two flights of stairs) than what is “limiting angina” for a 75-year-old (who would not try to run up two flights of stairs in any case). Another cardiologist said he specifically tried not to be influenced by co-morbidities that he knew were very prevalent among survivors of heart attacks, such as diabetes or stroke, and also consciously resisted an “ageism” bias, by not necessarily assessing the older patients as more impaired.

The six respiratory disease experts uniformly found the exercise to be easy, the scenarios plausible, and the instructions clear. They reported spending between 10 and 40 minutes assessing the three scenarios (median time was 10-15 minutes). Two of them, however, pointed out that the EQ-5D was problematic in conjunction with the specified severity levels of disease, in that the three-level structure of the instrument corresponded perfectly to the severity levels in the scenario. Several mentioned that a disease-specific index would be desirable, because it would be more sensitive to impairments related to respiratory disease than was the EQ-5D.

Several experts also said that they assumed they were being asked to assess chronic obstructive pulmonary disease (COPD) rather than chronic bronchitis alone, because shortness of breath was listed as a symptom in addition to cough and sputum. At the same time, several noted that chronic bronchitis and COPD had significant overlap, and that the characterization of the scenarios, with breathlessness included, was reasonable.

The cardiologists, in contrast to the respiratory experts, were less satisfied with the post-AMI categories that they were asked to assess. One assessor was confused as to whether the purpose of the exercise was to validate an approach to disease classification or to make a clinical judgment about the described health state. Another thought the array of possible post-AMI scenarios was a bit “off,” because Classes III and IV for angina did not appear in any of them. That expert recommended using one-paragraph patient vignettes that would take the physician assessor outside of the clinical classification system to consider patient experience of the condition more directly.

One of the cardiac experts was puzzled by the absence of the more severe classes of angina, and noted that medications did not always control it. Another noted that, while angina

and heart failure impose different limitations, in combination, those of congestive heart failure dominate. Two of the cardiologists mentioned that the major difference between younger and older persons suffering an AMI is the degree of anxiety/depression accompanying the event and disease. Older patients are more adaptive, whereas younger patients tend to be more upset about the change in their abilities and capacity to meet their responsibilities. Thus they assessed younger (<65) AMI survivors as more impaired on this dimension. Two of the cardiologists noted (similarly to the respiratory experts) that the correspondence between the three-level EQ-5D and the functional descriptors for the heart disease classes implied a direct mapping. One of these experts also indicated that the average level of impairments encompassed by the class descriptions obscured a wide variability of patient HRQL. Another cardiologist found both the clinical scenarios and the EQ-5D instrument too general and too crude to appropriately distinguish among health states. Three of the heart specialists reported spending about 20 minutes assessing the 11 scenarios for each of the two age groups, while one spent about 75 minutes.

Half of the respiratory specialists volunteered that the typical patient with chronic bronchitis was a smoker, and one said that bronchitis was rarely a stand-alone condition. One expert thought that the “mild chronic bronchitis” scenario described such mild symptoms that it characterized someone who would not meet the operational definition of chronic bronchitis. Another, on the other hand, thought that the assignment exercise would likely end up assessing the health states caused by air pollution too severely.

Last, one participant began the interview by commenting that clinicians are known to assess symptoms and functional capacities of patients very differently from patients themselves, and cautioned that physician proxy responses are not a very good substitute for patient self-assessments for any but the most general kinds of evaluations (such as economic analyses).

## **5.2 Key Sources of Uncertainty**

In general, the area of greatest uncertainty in regulatory analysis is often the risk assessment; i.e., the characterization of the types of health effects averted and the estimates of the number of cases avoided. These uncertainties may result from the emissions and air quality modeling and from the population projections used as well as from the underlying risk studies. A complete discussion of these issues is beyond the scope of this case study; related information can be found in the EPA source documents. EPA also provides information on the uncertainty in its cost estimates, as summarized in Section 2.0 above.

In terms of the analysis conducted by the case study team, each approach has certain limitations. All three approaches are affected by the limitations of the generic indices (i.e., the EQ-5D and the HUI-3) themselves as well as the data sources used to estimate average population health (MEPS and the Joint U.S.-Canada Survey of Health). The research reports used to develop our assessment provide more information on the sources of uncertainty in the underlying analysis.

As noted above, the experts involved in determining the EQ-5D attributes raised a number of issues related to their task, including the relationship between the disease descriptions

and the attribute descriptions, the differences between expert and patient judgments about disease impacts, the consideration of age-related or other co-morbidities, and the difficulties inherent in considering an “average” or “typical” case rather than an individual patient. A more thorough expert assignment process could address these issues by pre-testing the approach, working with the experts to ensure that they have a common understanding of the health conditions, EQ-5D attributes, and the task itself, and then following the initial assignment with a process for resolving (or better understanding) any inconsistencies in the results. Relying on patient, rather than expert, assignments was not possible given the time and resources available for this case study, but could also significantly alter the findings.

The application of the preliminary MEPS EQ-5D condition weights from Sullivan et al. (2005) involved a much simpler process than the expert assignment. However, we relied on preliminary estimates, and the estimates differ in the published analysis as does the suggested procedure for applying them. Some imprecision is introduced by our use of a mix of mean and median values, although the impact is likely to be small given the similarity of the estimates. The Sullivan et al. team also note that their research needs to be validated by condition-specific studies. In addition, in regulatory analysis, there is a need to distinguish between co-morbidities that may be averted by the regulatory action and those that may not. The Sullivan et al. regressions separate out co-morbidities that are associated with, but not caused by, the condition of interest. However, those that are essentially caused by the condition of interest may not be adequately addressed.<sup>55</sup> The Sullivan et al. analysis includes a variety of data that could be used in a more formal, quantitative analysis of uncertainty.

In our application of estimates from the Harvard Registry studies, we rely on a single study for each endpoint. However, as discussed in Section 3.4, other studies in that database report varying results for similarly defined health conditions, and a more comprehensive approach would consider the full range of values reported (such as, for example, the approach used in Hubbell, 2004).

In terms of the adequacy of the data for the HRQL assessment, we found that the available risk studies provided relatively little information on the severity of the cases of chronic bronchitis and nonfatal AMIs associated with exposure to PM<sub>2.5</sub>. If these cases are more or less severe than we assume in the HRQL assessment, our estimates of QALY losses may be under- or overstated. In addition, the association between PM<sub>2.5</sub> exposure and mortality risks is not well understood, leading to uncertainty in the lag and life expectancy assumptions used in the analysis. In particular, if preventable mortality disproportionately affects individuals with life-shortening pre-existing conditions, then our estimates of QALY losses may be overstated; we assume that the affected individuals would have the same life expectancy as the general U.S. population of the same age in the absence of pollution-induced mortality.

In addition, the estimates of average health include a relatively high prevalence of the conditions of concern in our analysis (chronic bronchitis and cardiac disease), especially among older individuals. If the regulation averts a new case of these diseases, the affected individuals may be in better health than the population averages. However, the difference in HRQL and life

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<sup>55</sup> Email from William Lawrence to Lisa Robinson, June 2, 2005.

expectancy will depend on the extent to which the prevalence of these diseases in the overall population is high enough to affect the mean results.

In addition, this analysis required comparing the “with condition” HRQL values to “without condition” values under both average and perfect health scenarios. Creating these comparisons involved developing assumptions about the basis of the “with condition” values and then adjusting these values as needed. This adjustment process, and the assumptions that underlie it, adds another source of uncertainty.

Finally, the cost-effectiveness calculations rely on EPA’s best estimates of regulatory costs, which the Agency suggests may be over or understated by about 20 percent. In adjusting the cost estimates to net out savings in health care costs, we rely on EPA’s estimates of medical costs which are incomplete and based on relatively old data. In addition, these estimates do not address the time losses associated with treatment or caregiving. The adjustment for benefits not included in the QALY measure includes only those benefits that could be quantified by EPA; the Agency notes that the nonroad regulations may lead to a number of other benefits that were difficult to quantify. We lack the data needed, however, to determine the direction and magnitude of any bias that may result from the combined effect of all the factors that lead to uncertainty in our estimates of HRQL, longevity, and cost-effectiveness.

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## APPENDIX A: EPA PILOT STUDIES OF COST-EFFECTIVENESS

In recent years, OMB and others have urged EPA to conduct cost-effectiveness analysis using HRQL-type measures, in addition to reporting costs per ton of emissions reduced and preparing a benefit-cost analysis that encompasses both health-related and other benefits. In response, Bryan Hubbell, an economist in EPA's Office of Air Quality Planning and Standards (within the Office of Air and Radiation) developed an approach for assessing the cost-effectiveness of a one microgram reduction in fine PM across the U.S. (Hubbell 2004). He recently updated and adapted his approach for EPA's Clean Air Interstate Rule (CAIR), and the resulting analysis was published as an appendix to the regulatory assessment for that rule (EPA 2005). EPA notes that the analysis is "preliminary and experimental" and does not necessarily establish a precedent for future cost-effectiveness analyses of EPA rules.

Because these two studies address pollution reductions that differ in magnitude from those attributable to the nonroad rule, the QALY and cost estimates are not comparable to the results reported in the main text of this paper. However, EPA's cost-effectiveness analyses use the same underlying epidemiological studies to assess the risks of PM-related mortality, chronic bronchitis, and nonfatal AMI, and are based on the same general analytic approach as the benefits analysis for the nonroad rule (i.e., EPA's BenMAP model). Hence we use some of the data developed for the Hubbell analyses in our case study, particularly the data on age at incidence, duration, disease progression post-AMI, and life expectancy post-AMI. These assumptions are discussed in detail earlier in this report.

The purpose of this appendix is to briefly summarize key features of the approach that EPA uses to value benefits in these analyses, in contrast to the approach used in this report. In both the 2004 and 2005 assessments, EPA uses values from the existing literature to assess the health-related quality of life (HRQL) impacts associated with nonfatal cases of chronic bronchitis and acute myocardial infarction, and also assesses life years lost to preventable mortality. While this approach is similar conceptually to our application of values from studies in the Harvard Registry, it differs in three significant ways.

First, EPA's approach compares the "with condition" values to perfect health for preventable mortality and to average health for the nonfatal endpoints. The end result is the sum of unadjusted life years gained from averted mortality and QALY-adjusted gains from averted morbidity. EPA refers to the resulting metric as "Morbidity Inclusive Life Years" or MILYs. EPA notes that "[t]his measure may be preferred to existing QALY aggregation approaches because it does not devalue life extensions in individuals with preexisting illnesses that reduce HRQL. However, the MILY measure is still based on life years and thus still inherently gives more weight to interventions that reduce mortality and morbidity impacts for younger populations with higher remaining life expectancy" (EPA 2005, p. G-2).

EPA developed this approach in response to OMB guidance, which states that:

*When CEA is performed in specific rulemaking contexts, you should be prepared to make appropriate adjustments to ensure fair treatment of all segments of the population.*

*Fairness is important in the choice and execution of effectiveness measures. For example, if QALYs are used to evaluate a lifesaving rule aimed at a population that happens to experience a high rate of disability (i.e., where the rule is not designed to affect the disability), the number of life years saved should not necessarily be diminished simply because the rule saves the lives of people with life-shortening disabilities. Both analytic simplicity and fairness suggest that the estimated number of life years saved for the disabled population should be based on average life expectancy information for the relevant age cohorts. More generally, when numeric adjustments are made for life expectancy or quality of life, analysts should prefer use of population averages rather than information derived from subgroups dominated by a particular demographic or income group. (OMB 2003, p. 13)*

EPA notes that this language can be read as suggesting the use of population averages (not adjusted for disabling or other conditions) for both the estimates of life expectancy and the estimates of HRQL. However, for the particular endpoints considered in EPA's analysis, it appears that the life expectancy of those affected by the regulations is not likely to differ from population averages.<sup>56</sup>

In contrast, this IOM case study uses a consistent approach for estimating “without condition” health for both mortality and morbidity. For both fatal and nonfatal effects, our base case estimates compare the “with condition” values to average age-adjusted population health, and our sensitivity analysis compares the “with condition” values to perfect health (i.e., a value of 1.0). Our approach to assessing life expectancy is very similar to the approach used in the EPA analysis, as discussed in the main text of this report and Appendix B. However, EPA uses a multiplicative approach to adjust survival rates for the effects of coronary disease, whereas our model uses an exponential approach.

The second major difference between EPA's analysis and the analysis used in the case study involves the treatment of uncertainty. EPA uses a probabilistic (Monte Carlo) model, which allows the Agency to examine the impacts of a range of values for many parameters. EPA reports its results as both mean values and as the 95 percent confidence interval surrounding these means. While we considered using a similar modeling approach, the available time and resources were not adequate to allow us to pursue this type of probabilistic analysis and the case study instead relies on mean values.

The third major difference relates to the studies used to assess the HRQL impacts of chronic bronchitis and acute myocardial infarction. EPA notes that: “[i]n general, consistent with the Gold et al. (1996) recommendations, we use weights obtained from a societal perspective when available. We explore several different sources for these weights to characterize some of the potential uncertainty in the QALY estimates. We follow many of the principles of the reference case analysis as defined in Gold et al. (1996), although in some cases we depart from the reference case approach when data limitations require us to do so (primarily in the selection of quality-of-life weights for morbidity endpoints).” EPA's search included studies that do not

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<sup>56</sup> There is some debate regarding whether PM-related mortality disproportionately affects individuals with pre-existing conditions as discussed in the main text of this report. Hubbell (2004) conducts sensitivity analysis to address this concern.

appear in the Harvard Registry used in the IOM case study (such studies include those that assess HRQL impacts but do not use the resulting data in a cost-effectiveness analysis). In addition, although in both analyses the criteria for selecting studies are derived at least in part from Gold et al. (1996), this IOM case study involved the development and application of several criteria that are not specifically referenced by EPA.

These different approaches to selecting studies resulting in somewhat different quality weights.

- For chronic bronchitis, EPA assigns a central tendency quality weight of 0.7 and assumes a triangular distribution bounded by weights of 0.5 and 0.9, based on Vos (1999) and Smith and Pesce (1994).<sup>57</sup> In the absence of chronic bronchitis, EPA assumes that the HRQL will follow a triangular distribution, with a central tendency of 0.95 and bounded by 0.9 and 1.0, following the practice used in Carrothers, Evans, and Graham (2002).
- For AMI, EPA estimates the quality weight as 0.605 during and immediately following the event, based on Vos (1999). For congestive heart failure and/or angina following the AMI, EPA uses a uniform distribution, ranging from 0.7 to 0.89 for angina only, from 0.80 to 0.89 for congestive heart failure only, and from 0.76 to 0.85 for individuals experiencing both conditions, based on Stinnett et al. (1996) and Kuntz et. al (1996). EPA assigns a weight of 0.93 to the HRQL for individuals who experience neither condition following a nonfatal AMI based on Kuntz (1996).

In presenting the results of the analysis, EPA separately reports each component used to construct the cost-effectiveness measure, including the estimates of life years gained from mortality risk reductions, the estimates of QALY gains for each of the morbidity endpoints, and the sum of these values (i.e., the total MILYs gained). To estimate net costs, EPA subtracts two items from the costs of regulatory compliance: the avoided costs of illness (including medical costs and lost earnings for the cases of chronic bronchitis and AMI, but not for preventable mortality), and the monetized value of those health and non-health impacts not captured in the MILY measure. Each of the resulting estimates is presented using both three and seven percent discount rates, and is accompanied by the estimates that bound the 95 confidence interval.

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<sup>57</sup> Vos (1999) is, in turn, based on Southard (1997).

## APPENDIX B: CALCULATION OF LIFE EXPECTANCY FOR AMI SURVIVORS

This appendix discusses our approach for using a standardized mortality ratio (SMR) to adjust life expectancy for those survivors of acute myocardial infarction (AMI) who do not develop congestive heart failure. The Excel spreadsheet models used in this case study calculate population average conditional survival rates on an annual basis for each year of age, based on CDC estimates of the probability of dying between ages  $x$  and  $x+1$  from the year 2000, referred to as  $q(x)$  in the CDC life tables (CDC 2002). We increase these death rates to reflect the impact of cardiac disease on life expectancy, using an exponential approach to apply an SMR of 1.52 from the literature, as discussed in Section 3.1.1 of this report. If  $d$  = the population average death rate and  $s$  = the SMR, then this exponential approach uses the formula  $1 - (1 - d)^s$  to calculate the “with condition” death rates.

This appendix provides two examples of the calculations: one for the year at incidence (when the probability of survival plus the probability of death equals 100 percent) and one for a future year (when the probability of survival plus the probability of death equals less than 100 percent because of the cumulative effect of the death rates in earlier years). Note that we use both the death and survival rates in our HRQL calculations, because we assume that deaths occur halfway through the year and hence get “half the QALY” for that year.

### Calculation for year 0

*Without* condition population average annual death rate, year zero = 0.005579<sup>a</sup>

*Without* condition survival rate =  $1 - 0.005579 = 0.994421$

With condition *death* rate =  $1 - (1 - 0.005579)^{1.52} = 0.008468$

With condition *survival* rate =  $1 - 0.008468 = 0.991532$

### Calculation for year 10

*Without* condition population average annual death rate, year 10 = 0.013646<sup>a</sup>

*Without* condition survival rate, year 10 = 0.904357

With condition *death* rate =  $1 - (1 - 0.013646)^{1.52} = 0.020668$

With condition *survival* rate = survival rate for prior year \* (1 – current year death rate) =  
 $0.876409 * (1 - 0.020668) = 0.858295$

<sup>a</sup> from CDC life tables for 2000, assumes 53 = age at incidence

**APPENDIX C: EQ-5D AND HUI-3 DOMAIN AND ATTRIBUTE DESCRIPTIONS**

<b>Exhibit C-1</b>		
<b>EQ-5D HEALTH STATUS CLASSIFICATION SYSTEM</b>		
<b>Domain</b>	<b>Attribute Level</b>	<b>Description</b>
<b>MOBILITY</b>	1	I have no problems in walking about
	2	I have some problems in walking about
	3	I am confined to bed
<b>SELF-CARE</b>	1	I have no problems with self-care
	2	I have some problems washing or dressing myself
	3	I am unable to wash or dress myself
<b>USUAL ACTIVITIES</b>	1	I have no problems with performing my usual activities (e.g., work, study, housework, family or leisure activities)
	2	I have some problems with performing my usual activities
	3	I am unable to perform my usual activities
<b>PAIN / DISCOMFORT</b>	1	I have no pain or discomfort
	2	I have moderate pain or discomfort
	3	I have extreme pain or discomfort
<b>ANXIETY / DEPRESSION</b>	1	I am not anxious or depressed
	2	I am moderately anxious or depressed
	3	I am extremely anxious or depressed

**Exhibit C-2**

**HEALTH UTILITIES INDEX MARK 3 (HUI-3) HEALTH STATUS CLASSIFICATION SYSTEM**

<b>Domain</b>	<b>Attribute Level</b>	<b>Description</b>
<b>VISION</b>	1	Able to see well enough to read ordinary newsprint and recognize a friend on the other side of the street, without glasses or contact lenses.
	2	Able to see well enough to read ordinary newsprint and recognize a friend on the other side of the street, but with glasses.
	3	Able to read ordinary newsprint with or without glasses but unable to recognize a friend on the other side of the street, even with glasses.
	4	Able to recognize a friend on the other side of the street with or without glasses but unable to read ordinary newsprint, even with glasses.
	5	Unable to read ordinary newsprint and unable to recognize a friend on the other side of the street, even with glasses.
	6	Unable to see at all.
<b>HEARING</b>	1	Able to hear what is said in a group conversation with at least three other people, without a hearing aid.
	2	Able to hear what is said in a conversation with one other person in a quiet room without a hearing aid, but requires a hearing aid to hear what is said in a group conversation with at least three other people.
	3	Able to hear what is said in a conversation with one other person in a quiet room with a hearing aid, and able to hear what is said in a group conversation with at least three other people, with a hearing aid.
	4	Able to hear what is said in a conversation with one other person in a quiet room, without a hearing aid, but unable to hear what is said in a group conversation with at least three other people even with a hearing aid.
	5	Able to hear what is said in a conversation with one other person in a quiet room with a hearing aid, but unable to hear what is said in a group conversation with at least three other people even with a hearing aid.
	6	Unable to hear at all.
<b>SPEECH</b>	1	Able to be understood completely when speaking with strangers or friends.
	2	Able to be understood partially when speaking with strangers but able to be understood completely when speaking with people who know me well.
	3	Able to be understood partially when speaking with strangers or people who know me well.
	4	Unable to be understood when speaking with strangers but able to be understood partially by people who know me well.
	5	Unable to be understood when speaking to other people (or unable to speak at all).
<b>AMBULATION</b>	1	Able to walk around the neighborhood without difficulty, and without walking equipment.
	2	Able to walk around the neighborhood with difficulty; but does not require walking equipment or the help of another person.
	3	Able to walk around the neighborhood with walking equipment, but without the help of another person.
	4	Able to walk only short distances with walking equipment, and requires a wheelchair to get around the neighborhood.

**Exhibit C-2**

**HEALTH UTILITIES INDEX MARK 3 (HUI-3) HEALTH STATUS CLASSIFICATION SYSTEM**

	5	Unable to walk alone, even with walking equipment. Able to walk short distances with the help of another person, and requires a wheelchair to get around the neighborhood.
	6	Cannot walk at all.
<b>DEXTERITY</b>	1	Full use of two hands and ten fingers.
	2	Limitations in the use of hands or fingers, but does not require special tools or help of another person.
	3	Limitations in the use of hands or fingers, is independent with use of special tools (does not require the help of another person).
	4	Limitations in the use of hands or fingers, requires the help of another person for some tasks (not independent even with use of special tools).
	5	Limitations in use of hands or fingers, requires the help of another person for most tasks (not independent even with use of special tools).
	6	Limitations in use of hands or fingers, requires the help of another person for all tasks (not independent even with use of special tools).
<b>EMOTION</b>	1	Happy and interested in life.
	2	Somewhat happy.
	3	Somewhat unhappy.
	4	Very unhappy.
	5	So unhappy that life is not worthwhile.
<b>COGNITION</b>	1	Able to remember most things, think clearly and solve day to day problems.
	2	Able to remember most things, but have a little difficulty when trying to think and solve day to day problems.
	3	Somewhat forgetful, but able to think clearly and solve day to day problems.
	4	Somewhat forgetful, and have a little difficulty when trying to think or solve day to day problems.
	5	Very forgetful, and have great difficulty when trying to think or solve day to day problems.
	6	Unable to remember anything at all, and unable to think or solve day to day problems.
<b>PAIN</b>	1	Free of pain and discomfort.
	2	Mild to moderate pain that prevents no activities.
	3	Moderate pain that prevents a few activities.
	4	Moderate to severe pain that prevents some activities.
	5	Severe pain that prevents most activities.