UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

EPA-SAB-CASAC-LTR-93-014

September 30, 1993

OFFICE OF THE ADMINISTRATOR
SCIENCE ADVISORY BOARD

Honorable Carol M. Browner
Administrator
U.S. Environmental Protection Agency
401 M St. S.W.
Washington, D.C. 20460

Subject: Review of Draft Strategy for Alternative Fuels Research

Dear Ms. Browner:

The Clean Air Scientific Advisory Committee (CASAC) of EPA's Science Advisory Board (SAB) met on June 29 and 30, 1993, to review the Office of Research and Development's (ORD's) draft strategy for research on alternative fuels. The Committee is pleased with this attempt to capture the mix of research and development activities necessary to assess alternative fuels. While we have made many substantive comments (see attachment) on the technical content of the document, we would like to reiterate our major comment on the overall concept --- the allocation of adequate resources for such an effort will determine its success or failure prior to its implementation.

We thank you for the opportunity to participate in this research strategy review and look forward to hearing about plans for its implementation.

Sincerely,

George T. Wolff

George T. Wolff
Clean Air Scientific Advisory Committee

CONTROL SLIP FOR OFFICE OF EXECUTIVE CORRESPONDENCE

TROL NO : AX9310525

DUE DATE: 11/30/93

M : WOLFF, GEORGE T.
SCIENCE ADVISORY BOARD

CORRES. DATE: 09/30/93
RECEIVED: 10/13/93

ASSIGNED: 10/14/93

LUTATION : DEAR MR. WOLFF

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BJECT : RPT-DRAFT STRATEGY FOR ALTERNATIVE FUEL RESEARCH
(SAB-CASAC-LTR-93-014)

IGNATURE : ADMINISTRATOR

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IMS: JF

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

JAN 14 1994

THE ADMINISTRATOR

Dr. George T. Wolff
Clean Air Scientific Advisory Committee
U.S. Environmental Protection Agency
401 M Street, S.W.
Washington, D.C. 20460

SUBJECT: Report Draft Strategy for Alternative Fuel Research
(SAB-CASAC-LTR-93-014)

Dear Dr. Wolff:

We are very grateful for the Clean Air Scientific Advisory Committee's (CASAC) thorough review of the Alternative Fuels Research Strategy. We particularly appreciate both the breadth and depth of expertise that the Committee brought to bear. The Office of Research and Development (ORD) is currently revising the Alternative Fuels Research Strategy, taking advantage of the Committee's insightful comments.

In your letter, you correctly remark that the success or failure of this research program will depend on allocation of adequate resources. As you are aware, there are numerous competing resource priorities; and we continue to examine our resource allocations. In addition, we are seeking ways to leverage scarce resources through collaboration with other public and private institutions that might provide joint funding for this important research. Having an improved research strategy, due to your efforts, is critical in ensuring that the resources are allocated to the best science possible.

Thank you again.

Sincerely,

Carol M. Browner

M - MM
P - SL

Comments on "Alternative Fuels Research Strategy" EPA/600/AP-92/002, December 1992, External Review Draft

Charge for the Review of the Alternative Fuels Research Strategy Document Review Questions:

1. Is the risk-assessment framework the best approach for fostering cooperation and coordination among the various public and private organizations that may wish to conduct scientific research on issues related to the subject of the document? If not, what alternative approach would be preferable?

Goldstein:

1. Philosophically, I agree with the use of a risk-assessment framework for integrating and directing a broadly scoped, complex environmental research program. However, the framework included in the plan is very general. In addition, instructions for its implementation are imprecise. If it is left to each organization to decide independently how it will address the subject matter, then it is highly unlikely that the overall effort will be integrated and efficient. The strategy needs to contain more specific decisions such as the selection of the South Coast Air Basin as the geographical region to focus research. For air pollution effects on terrestrial vegetation, the strategy should target specific plant communities. Essentially, the situation that exists is somewhat analogous to having the Allied forces in World War II choose Normandy as the area for the invasion of Europe, but then leaving each country decide for itself the beach and date it wants to land its troops.

Colome:

I found the conceptual approach to be very useful. A risk framework is particularly helpful for developing research priorities for applied environmental research. The paradigm clearly identifies gaps in the logic chain needed to understand technological risks. If a research program were completed using this framework it would provide an opportunity to compare various policy options with good information on the risk side of the equation.

Unfortunately, while the conceptual framework is useful, the total funding level available to address the issue of environmental risks form alternative fuels is not sufficient to fill in the framework. Unless the funding situation is improved, the risk framework will primarily serve to underscore the significant gaps in our understanding.

Miller:

A risk assessment framework is, in the opinion of this reviewer, the best approach for fostering cooperation and coordination among various research organizations which are addressing a common public health issue. The power of the approach is highlighted by an orientation related to an exposure-- dose -- response paradigm. This orientation provides various research groups with the opportunity to see more clearly which parts of the overall puzzle are being addressed and to design experiments to fill current data gaps. It also provides for an iterative approach for future risk assessments.

Winner:

The Risk Assessment framework is not explicitly designed to foster interagency cooperation needed to develop focused, scientific efforts. The Risk Assessment framework, however, could bring perspectives and resources from an array of agencies if this goal was designed at the onset. One approach to developing interagency participation is to bring other relevant agencies into the idea at the Research Program planning stage. Early inclusion gives other agencies a sense of co-ownership, can help secure commitments for resources, and allows agencies to identify their own work areas. There is little evidence of interagency participation at this point.

Utell:

The risk assessment framework is an effective approach for the organization of this document. I found it a useful way to present the material.

Liu:

The general approach of using risk assessment to provide a framework for a research strategy on alternative fuels appears to be a rational and reasonable one. The difficulty is that many of the health and environmental risks are difficult to quantify

or the information is either totally absent or insufficient to provide quantitative risk analysis results. Nevertheless, one must pursue this strategy, and do the best one can in setting research priorities based on the relative risk assessment approach.

In pursuing this strategy, one must keep in mind the finite resources that is available to carry out the research and the limited time frame in which the work must be done. EPA must perform high quality work that is relevant to the question at hand. At the same time, the agency must fund fundamental, basic research that will feed into this risk assessment framework.

Question: How does the agency plan to carry out its research. Does it plan to rely on its traditional sources of research suppliers for this work? What is the mix between work done by in-house personnel, research at Universities and for-profit or non-profit research organizations? What is the mix for the current EPA programs and what is the likely mix for the Alternate Fuels program?

Comment on Stationary Source Characterization

o Risk Assessment Research Framework: The framework of doing risk analysis taking into account risks associated with feed stock, production, storage/distribution and fuel use appears to be a reasonable one. The problems are obviously very complicated. How do you plan on scoping out the problem, so that resources are not spent unnecessarily on risks that are relatively minor and/or unimportant? What is your approach that will insure that major risks will be uncovered, including risks to workers in an occupational setting and risks associated with accidental, and perhaps intentional misuse of the fuel?

o Background and Rationale - Exposure Assessment: When you at looking at alternate fuels that will provide better air quality, you are looking at reduced exposure risk to the public. On the other hand there may be increased risk of occupational exposures associated with the production, storage and distribution of the fuel. Let us say that by using alternate fuel X, you decrease the risk of the public dying of cancer by 100 cases per year, but you increase the risk to workers producing and handling the fuel by 50 cases per year. So, you have a net gain of risk reduction by 50 and you say that is worthwhile. What if the numbers are turned around where you

reduce the pubic risk by 50, but increase the occupational risk by 100. Would you attempt to make a value judgment and say that one must achieve parity, or that it is acceptable to have a higher occupational risk than a public exposure risk, because one is paid for one does, while the other, does not?

2. Does the document adequately state research priorities by fuel type and scientific discipline? If not, can the CASAC provide a consensus view of these priorities?

Goldstein:

I think that the statement of priorities is by and large good. The priorities should however be integrated and summarized, using a table and flow chart in the executive summary. I cannot tell the difference between the definitions given for priorities one and two (see bottom of page 7-2). Are such definitions necessary? Can one just take priority one as being the most important, priority two the next, and so on?

The priorities are stated as objectives. The strategy needs to define research products and production time schedules.

With respect to terrestrial ecosystem effects, I feel too great a relative priority is placed on dose response research in chambers (pages 2-96). If one is interested in only a few plant species, a few pollutants and a limited number of environmental exposure conditions, then a dose response approach is highly efficient. However, if one is dealing with many plant and pollutant species and the environmental conditions are highly variable, then a mechanistic-based approach will be most efficient in the long run. A strategy should be designed that allows one to emphasize mechanistic studies that also yield dose response information. In addition, the time has come to start implementing field and microcosm experimental designs.

I do not understand the second part of this question. I do not believe in management by committee, least of all an advisory committee.

Colome:

The document lacks a general framework for developing research priorities across fuel types. It would be useful to determine early during the assessment process whether certain links in the risk chain provide most of the uncertainty and whether certain fuel types dominate the health or environmental risk. A high potential for deleterious effects could result from high exposures or toxicity. A preliminary hazard evaluation would help rank the potential for exposure and health impact and the role of uncertainty in limiting our understanding. This scoping exercise is particularly important given the limited resources available for this program of research.

One strategy that I did not see considered is to take advantage of the evaluation opportunities presented by natural experiments such as spills or individual legislative actions. These might be useful for evaluation of exposures and/or effects.

The priorities stated for human exposure research are reasonable and justified.

Miller:

The research priorities by fuel type and scientific discipline for health effects are stated very broadly. In fact, the priorities in research are described so broadly that it would be difficult for most reviewers to take exception to the priorities as stated in the document. However, as the material contained in the research strategy document indicates, significant research is missing on so many aspects of the various compounds that a clear prioritization across compounds for more in depth health effects research is not warranted at this time. Moreover, it would be hard for any group, including CASAC, to reach agreement on a different set of priorities.

Winner:

The general features of research priority classes 1, 2, 3, and longer term are defined (pg. 2-79, and at the lead-in to each Research Needs section for each fuel type). Research objectives are clearly spelled out for each fuel type and the objectives are labeled with a priority classification that is easily understood. However, several concerns exist:

1. I am not sure that the identification of 4 priority classes is helpful as only classes 1 and 2 will likely be pursued.

2. There is a certain redundancy in pursuing each fuel type independently and makes the document longer than need be, cumbersome to read, and buries important data, rationale, and research needs.

3. There may be significant disagreement on research objectives for each fuel type and the assigned level of priority.

4. A focused Risk Assessment framework would help provide rationale for prioritization of research objectives.

Utell:

The document adequately states research priorities by fuel type. It suffered a bit from being a wish list given the proposed budget. But in any case, I could not define a better way to do it.

Liu:

Research Needs: I have no problem with your stated research needs in stationary source characterization.

3. Is the Background and Rationale for each fuel adequately stated to support the research needs identified for that fuel?

Goldstein: Yes.

Colome:

Generally, yes. These sections have considerable redundancy from one fuel type to another and could be shortened.

Miller:

The Background and Rationale sections for each fuel are generally adequately covered to support the research needs identified for that fuel. In my Specific Comments, a number of publications in the 1989-1992 time period are cited that provide additional information that should be included in the document. Some of the newer studies do in fact provide information that would alter the recommended research strategy for methanol of these more recent publications in the Specific Comments portion of my review.

Winner:

The Background and Rationale material presented for each fuel type simply convinces the reader that not much is known about emissions from alternative fuel combustion. Thus, there is a general rationale developed around the absence of information. However, the B&R section does not synthesize that which is known and draw thinking towards research needs that, taken together, form an integrated program.

Utell:

The background and rationale for each fuel is adequate in supporting the subsequent research needs. In fact, it was at times too extensive.

4. Does the document provide sufficient information under the Research Needs sections to guide decision-makers in the allocation of funding for research on the issues identified in the document?

Goldstein:

No. Without a description of specific products, how they will be used in the risk assessment, their cost, and when they will be delivered, there is no way for the decision-maker to rationally allocate funding.

Colome:

The document does not offer a ranking of projects between fuels. There are many Priority #1 research projects listed but there is no effective structure for ranking among the highest priority projects suggested for the various alternative fuels. Since the funding available is unlikely to permit near-term support of projects beyond the Priority #1 category, the document will not be able to guide the allocation of research funding over the next few critical years.

Miller:

Overall, the document provides sufficient information to guide decision makers in the identification of areas most important for funding. However, the relative magnitude of the research dollar allocation between areas would be difficult to establish based upon the material presented in the document relative to, for example, health effects research only. The relative apportionment across types of research categories such as exposure, analytical methodology, human health effects, ecosystem effects, global warming, mobile sources, etc., would be difficult to do based upon the material contained in the document. Given limited resources, some attempt should be made to rank issues across these types of categories thereby identifying the highest priority areas overall.

Winner:

The Research Needs section will leave decision makers with the idea that not much is known about potential changes in air quality caused by increased use of alternative fuels. The reader will also feel that since so much research is needed, and no mechanism for application of research to relevant questions is provided, that it will be difficult to make decisions about funding priorities and directions. Without a specific regulatory/scientific purpose, funding allocations will appear to be arbitrary.

Utell:

The major deficiency under the research needs section relates to integrating realistic exposure concentrations with health effects studies. As discussed above, this needs to be incorporated into the document.

5. Are there significant facts omitted from the Strategy that would alter the priorities suggested by the document as it currently stands? Does the level of detail appropriately match the actual state of the science for the various fuels and disciplines covered in the document?

Goldstein:

I have already pointed out what I consider to be deficiencies in the formulation of the priorities. The level of detail is fine. I think several paragraphs can be added to summarize current deficiencies in the state-of-science understanding of plant community response to air pollution.

Colome:

The document was not designed as a thorough literature review. The knowledge, opinion, and experience of the staff went into developing and ranking the research priorities contained in the document. Not all of that experience was explicitly laid out in the document. I have no problem with that given the necessity of utilizing expert opinion to derive research priorities. As stated in number 4 above, the problem with the document is that it provides little guidance for establishing priorities across fuels among the Priority #1 projects.

Miller:

As noted earlier, more recent publications would alter some aspects of the Strategy. That is to say that the research cited through 1989 would primarily support the generation of the document in its current form. The document is broad sweeping in its treatment of all of the health effects research areas so that comments on detail appropriately matched to the state of the science do not appear to be warranted.

Winner:

The level of detail in the Research Plan ranges from highly technical graphs, to summary table, to general ideas and concepts. The wide range of detail is fine. The

specific area of ecosystem/vegetation research is poorly developed. Work by the Corvallis Lab has shown that plant growth is affected by ambient concentrations of formaldehyde found in southern California. The idea that ambient levels of formaldehyde could inhibit plant growth is important justification for continuing ecosystem research, but these data are omitted from the Research Plan.

Utell:

The major facts omitted from the Strategy relate to laying out the actual anticipated exposure concentrations. Without this effort, it is difficult for the reader to appreciate the significance of any proposed research.

General Questions:

1. Is the purpose of the Strategy -- "to lay a foundation for developing the scientific information needed to compare the benefits and risks of alternative motor vehicle fuels to those of conventional gasoline and diesel" -- appropriate and conceptually clear? Is such a purpose practicable? achievable?

Goldstein:

The purpose of the strategy is appropriate and conceptually clear. The objective is practicable. Achievability depends on available resources.

Colome:

Whether or not we will ever be able to objectively compare the benefits and risks of alternative fuels to conventional fuels is open to debate where reasonable opinions will differ. However, this process should be seen as a dynamic one and the risk framework offered in the document is useful for structuring and directing that process. As stated previously, the greatest threat to achieving the purpose of the document is the very modest budget available to address the research agenda contained in the document.

Miller:

The general purpose of the Research Strategy is adequately conveyed in the written material. Moreover, the identification of research needs and other discussions repeatedly refer back to the overall purpose, so that the document is effective at conveying how proposed research relates to the overall purpose of the Research Strategy document. Given the large combination of potential alternative fuels and fuel additives, the full evaluation of potential effects is not realistically achievable. However, the document does provide an overall course to follow that will enhance the probability of relevant information being available to make major decisions among categories. The document provides a guideline for identifying options rather than a basis for concrete decisions and choices.

Winner:

The statement of purpose for the Research plan is too general to be useful. Although the statement is clear and easily understood, the goal of laying a foundation for developing the scientific information needed to compare the benefits and risks of alternative fuels does not convey the specific purpose of the alternative fuels program. Thus, although parts of the statement of purpose can be achieved, the goal is to general to be practicable .

2. Does the Strategy achieve its goals laying such a foundation? If not, in what respects does it fail or fall short? What specifically would be needed to make it possible to achieve its goal?

Goldstein:

It makes a good start. As stated above, more specificity is needed with respect to structure and instructions for implementation. The first step would be to draw up a table or chart that summarizes all priorities and their interrelationship. I also believe it would be preferable to define the strategy and priorities in terms of specific deliverables instead of open-ended objectives.

Colome:

This is a well written thoughtfully presented document that provides good fuel-specific foundations for establishing funding priorities for research needed to address the health risks of alternative fuels. As stated previously, the document falls short only for its lack of providing a framework for developing a priority listing among the alternative fuels, i.e., which fuel should be addressed first.

Miller:

The Strategy tends to achieve the goal of laying the foundation for developing scientific information that is needed, but it falls short in realistically addressing the time frame needed to address the critical research needs. Also, the document fails to convey to decision makers responsible for the allocation of funds the amount of the funds that are actually needed to achieve a comprehensive research program. In order to achieve this goal a more detailed research document for the given areas would be desirable, but in lieu of that, a clearer identification of the longevity of the research programs should be identified up front in the Research Strategy.

Winner:

To achieve the goal of laying an understanding to serve as a basis for comparisons between impacts of using conventional vs alternative fuels, the Research Statement should be more focused and include specific risk assessments that require information that will be used in direct ways.

Panel Specific Comments

Mauderly:

List of Abbreviations: Pg. xxiv: "Insert TSCA (Toxic Substances Control Act).

Pefley:

Executive Summary: Based on economic factors there is a fuel usage implementation scenario that should be recognized and used to focus the phasing of ORD's investigations. From my experience, that fuel usage implementation schedule

suggests studies as follows: baseline gasoline and diesel studies, reformulated gasolines, M-85, FFV fuels including M-100 and E-100, reformed methanol (CO + 2H2) and natural gas.

Note that I include reformed methanol for it could well prove to be a way of reducing formaldehyde at the combustion source and subsequently allowing the production of an ultra-low emission vehicle operating on M-100. It deserves consideration.

Table E-1. Types of Potential Inhalation Health Effects of Individual Chemicals or Complex Mixtures Related to Conventional and Alternative Fuels Use, Pg. E-11: Shouldn't Item 1 be conventional fuels? Unless these have been fully evaluated as baselines, EPA can be accused of making an attack on alternative fuels without understanding the baselines. You so state on lines 27-30, page E-29.

Miller:

Executive Summary, Pg. E-1, line 12: References are made to risk benefit and cost benefit analysis as part of the need for the document. However, comparative risk activities are also a likely use for the research contained in this strategy.

Miller:

Executive Summary, Pg. E-16, lines 3-11: The Office of Mobil Source's estimates of U.S. cancer incidence for gasoline related compounds and the estimation of 50% of the carcinogenic air toxics problem being attributable to gasoline and diesel exposures are provided as "a basis of fact." However, the analyses underlying these estimates have significant uncertainty, and the use of 95% upper confidence limits on the risk tends to "skew perception of risk."

Wood:

Executive Summary, Pg. E-16, lines 17-18: "...adverse effects such as vertigo are associated with high levels of gasoline vapors, but are of minimal concern..." I take exception to this stance. If there is no other documented adverse effect of exposure, narcosis or irritation becomes the critical endpoint. Thus, data on narcosis in the first tier of testing permits an early estimate of an exposure limit value so based and an opportunity to evaluate explicitly whether it is adequate to protect against other

toxicities that might result from a lifetime of exposure. Furthermore, "topping off" tanks can result in saturation of volatile emission control systems, and exposure in the passenger compartment. (I drive an older car, I have seen this first hand). You would not want a solvent inebriated driver on the road, displaying impaired reaction time, at 55 mile per hour. Changing fuel formulations may change the risks associated with passenger compartment exposures.

Wood:

Fuel-Specific Scientific Issues, Methanol, Health Issues, Pg. E-21, line 10: respiratory tract effects and eye irritation...

Miller:

Executive Summary, Pg. E-19, line 24: The pharmacokinetic studies of methanol exposure in primates indicate that the risk from expected methanol exposure levels associated with alternative fuels is indeed minimal.

Colome:

Executive Summary, Pg. E-22, lines 27-34: This section is not clear. If my interpretation is correct, the sentence ending on line 33 should add the following clause: "which is emitted during combustion of ethanol." Is it known yet whether 'significant' amounts of formaldehyde are emitted from methanol-fueled vehicles?

Miller:

Executive Summary, Pg. E-26, line 8: The statement that formaldehyde can cause cancer needs to be clarified that this has been demonstrated in laboratory animals. the evidence has been suggestive in epidemiological studies relative to lung cancer, and EPA has classified formaldehyde as a probable human carcinogen.

Miller:

Executive Summary, Pg. E-27, lines 5-12: While the reductions in carbon dioxide would be significant for CNG vehicles, the hear retention potency difference between methane and carbon dioxide does not allow this reviewer to infer that, as stated on page 9, "overall, vehicle related greenhouse gas emission from CNG vehicles will probably be reduced."

Colome:

Executive Summary, Pg. E-29, lines 21-23: This is an important and well-phrased statement.

Miller:

1.0 Introduction, 1.3 Regulatory Background, Pg. 1-4, Table 1-1: As noted in Table 1-1, methanol utilization in gasoline is negligible. Thus, unless compelling reasons eliminate other alternative fuels from consideration, the priority for methanol research should probably be relatively low.

Miller:

1.0 Introduction, 1.3 Regulatory Background, Pg. 1-5, line 23: Strike the word "has".

Colome:

1.3 Regulatory Background, Pg. 1-6, lines 29-31: It would be useful to include a line or two explaining the principles of vapor recovery. This important control strategy receives less attention in this section than it deserves.

Suter:

1.4 Introduction to Risk Assessment Framework for Fuels, Pg. 1-9: The reason for focusing on effects of air pollution on plants and of spills on aquatic biota should be stated. It may be because aquatic oil spills and ozone effects on plants are the major ecorisk issues with respect to conventional motor fuels, or because a screening assessment was done which concluded that these were the major issues for all motor fuels.

Suter:

Figure 1-2. Generic major risk assessment pathways of motor fuel production, distribution, storage, and use. Pg. 1-11: Figure 1-2 is a good basic conceptual model. I would change the word "Ecosystem" to "Ecological". You may wish to address ecological risks at the population scale or the regional scale, not necessarily the ecosystem scale.

Suter:

Pg. 1-13, lines 13-16: Risk assessment is not what comes after exposure assessment and effects assessment. Conventionally it is risk characterization, and in the rest of the document it is scientific assessment. Also, I may have missed it, but I did not see a definition of scientific assessment.

Miller:

1.4.1 Exposure Assessment, Pg. 1-14, line 26: Determining the amount of a pollutant that enters an exposed subject is identified as an exposure assessment activity; however, the overlap to dose response is clearly great, and the characterization of dose is more likely to be done in the type of detail useful for risk assessment if it is a part of health effect studies.

Colome:

1.4.1 Exposure Assessment, Pg. 1-15, lines 1-9: The need for sequentially derived information is described effectively in his section.

Suter:

1.4.1 Exposure Assessment, Pg. 1-15, lines 2-4: Implies that exposure assessment is always based on measurement of concentrations. As you are obviously aware, there is not always a measurement phase in the development of exposure assessment. Some clarification is needed.

Suter:

1.4.1.1 Source Characterization, Pg. 1-15, line 21: Certainly for aquatic effects, mobile sources (e.g., tankers) are important emissions sources.

Miller:

1.4.1.1.1 Emissions from Feedstock and Fuel Production, Storage, and Distribution, Pg. 1-16, line 20: EPA would be well advised to dismiss consideration of the use of oil shale as a feed stock for the production of alternative fuels given past national experiences related to shale oil retort.

Miller:

1.4.1.1.1 Emissions from Feedstock and Fuel Production, Storage, and Distribution--Production, Pg. 1-19, lines 13-16: The point made here concerning an adequate determination of baseline characteristics cannot be overstated. The comparison of alternative fuels and their by-products in the form of emissions must have a solid data base for comparison so that one problem is not substituted for another.

Miller:

1.4.1.1.2 Emissions Related to Fuel Use--Mobile Source Emissions, Pg. 1-22, line 2: Why is 70 degrees F implied to be a global minima relative to CO emission rates from motor vehicles?

Miller:

1.4.1.1.1 Emissions from Feedstock and Fuel Production, Storage, and Distribution--Production, Pg. 1-24, lines 5-11: Given the high percentage of total VOC and of NOx emissions attributable to non-road engines, this reviewer questions the wisdom of deleting these sources from consideration for the use of alternative fuels. This is particularly true since these are contributing sources for ozone formation and the national ozone problem is of such magnitude that every avenue of reducing ozone needs to be explored.

Miller:

1.4.1.2.2 Soil and Groundwater Fate, Pg. 1-27, lines 6 and 7: The case for quantifying changes resulting from a fuel without site-specific parametrization is largely overstated. The utility of this approach is doubtful.

Miller:

1.4.1.3.1 Human Exposure Assessment, Pg. 1-29, lines 1-7: Given the limited resources that will be applied to the alternative fuels health effects research issues, this reviewer does not see the value of expending resources to investigate intentional/accidental swallowing episodes. Such investigations are outside of the mainstream of the necessary research activities for a focused alternative fuels

research strategy. Rather, some expenditures on labeling and container safeguards would appear to be more useful.

Miller:

1.4.1.3.1 Human Exposure Assessment, Pg. 1-30, lines 6-9: There is no compelling reason to expect that initial studies with alternative fuels should be conducted at probable human exposure levels. To the contrary, high exposure levels will be needed, and only when effects are seen that are likely to be of a serious and irreversible nature will it be appropriate to expend resources to conduct concentration response studies at lower levels. Even in this instance, if chronic effects are of concern, then extrapolation issues will arise because the studies will need to be conducted at still higher exposure levels than what humans will likely encounter. The current text comments are more appropriate for acute exposure studies, particularly those involving human subjects.

Suter:

1.4.1.3.2 Biota Exposure Assessment--Terrestrial Ecosystem Exposure, Pg. 1-31: The section on terrestrial ecosystem exposure suggests that an appropriate approach might be derived from NAPAP models. I agree that it is not appropriate to start from scratch. This idea does not appear in the aquatic section, but for exposures to fuel spills the EPA should start with existing spill models such as the DOI's Type A NRDA model.

Miller:

1.4.2.1 Human Health Effects, Pg. 1-36, lines 21-28: It should be noted that mimicking an exposure scenario in pattern but not necessarily in magnitude can yield useful information for assessment of human health; moreover, such elevations in patterns are typically necessary in toxicologic studies.

Schreck:

1.0 Introduction, 1.4 Introduction to Risk Assessment Framework, 1.4.2 Effects Assessment, 1.4.2.1 Human Health Effects--Pg. 1-36 line 25: "Inhalation is the most probable route of exposure for the general public and therefore Table 1-4 is a good

overview of the risk problems, but ... dermal exposure (mentioned in line 27) should not be minimized as a route for real world exposure."

Mauderly:

Introduction: 1.4.2 Effects Assessment, 1.4.2.1 Human Health Effects, Pg. 1-36, line 30: It is not made clear, here or elsewhere, to what extent an emphasis is to be made on "replication of published results." This is an open statement with high impact; for example, should all key earlier results be "replicated."

Wood:

Table 1-4. Types of Potential Inhalation Health Effects of Individual Chemicals or Complex Mixtures Related to Conventional and Alternative Fuels Use, Pg. 1-37: II. Complex Mixtures of Conventional Fuels...respiratory tract effects and behavioral effects.

Schreck:

Pg. 1-38 lines 1-16: This entire paragraph addresses the design of research well, namely, using biologically-based dose response models to determine the relevance of the effects to humans, basing research bioassays on the market penetration of various fuels (since some may never become commercially viable), and the idea of targeting populations in cities before and after fuel switching for tests of microenvironmental exposures, symptoms, etc.

Schreck:

Pg. 1-39-Table 1-5: Although I generally agree with the entries in Table 1-5, I would reorient priorities in some cases. Specifically, I think under "Fuels," Reformulated Gasoline should be given a higher priority because its widespread use is imminent. "Pollution Sources" is fine. "Human Exposure Scenarios" should consider refueling a higher priority, perhaps second under Microenvironments. Under Dermal ... occupational exposures will be the major source of dermal contact with these fuels rather than incidental contacts.

Miller:

1.4.2.1.2 First Priority--Pharmacokinetic Evaluations, Pg. 1-40, line 31: While this reviewer agrees that pharmacokinetic evaluations are extremely important, the myriad of emissions from alternative fuels and from recombinated fuels is no different than the magnitude of the problem of trying to address the pharmacokinetics of unleaded gasoline. Great care must be taken to prune the list of potential aspects of the pharmacokinetic modeling if any inroads are to be made on the overall problem.

Wood:

1.4.2.1.2 First Priority--Pharmacokinetic Evaluations: This is misplaced. Hazard ID should come first.

Schreck:

1.4.2.1.3 Second Priority--Dose Response Evaluations--Pg. I-42, lines 6-16: "The question arises, 'how much bioactive material will be found in the exhaust of these vehicles after they are fitted with custom designed catalysts.' This approach was effective with diesel exhaust because organics were plentiful, but these alternative fuels are lower molecular weight and in general 'burn clean' leaving less complex organic material in the exhaust even before catalytic after treatment."

Miller:

1.4.2.1.3 Second Priority--Dose-Response Evaluations, Pg. 1-42, line 10: It would be helpful if some specificity as to the nature of the type of short term assays that are proposed to be used would be given. The potential list of *in vitro* studies is extremely long and insight is going to be needed on pruning it to match with likely target tissues and cells from the relevant route of exposure--inhalation.

Suter:

1.4.5.2 Ecosystem Risk Priorities, Pg. 1-53, lines 18-22: These sentences are examples of why this strategy is frustrating to review. Nothing is "fully understood." "Source characterization, environmental fate, and biota exposure and effects" covers all aspects of ecological risk assessment. In other words, the conclusion is that everything needs to be researched and always will need to be researched because full understanding is required but can never be achieved. I know that you have not

completed the prioritization yet, but you should have a consistent strategy for identifying research topics and then for performing the prioritization.

Suter:

1.4.5.2 Ecosystem Risk Priorities, Pg. 1-54, lines 14-21: I heartily agree with the call for screening assessments that appears in these lines.

Suter:

1.4.5.3 Global Climate Change Priorities, Pg. 1-54: This section vaguely refers to "another EPA program" creating the impression that the linkage between this program and efforts to assess risks from global climate change are undefined. If your research is to be useful to that other program, you need to involve them.

Pefley:

2.0 Conventional Fuels, Pg. 2-1: The statement is made "Conventional petroleum-based fuels have a relatively long history of use and experience, yet much remains to be learned about their effects on the environment, humans and biota." Suggested insert: "By today's standards, if they were brought to market they would be presented as toxic substances and carry appropriate warnings."

Suter:

2.1.1.2.3 Surface Water Fate, Pg. 2-10, lines 24 and 25: Suggests that studies of all individual components of conventional fuels are required. That is a futile research program both because the funds are not available and because the fate of individual chemicals is affected by the carrier (i.e., the spilled fuel or feed stock). Unless you have evidence that specific components are significant contributors to risk, focus on the fate of the whole material and then on major fractions. (This approach seems to be suggested later in the document).

Mauderly:

2.0 Conventional Fuels, 2.1.2 Effects Assessment, 2.1.2.1 Human Health Effects, Pg. 2-15, lines 12-16: The body of research referenced (DOE, API) dealt primarily with fuels and process streams; little, if any emphasis was placed on combustion products in the studies of alternate fuels.

Schreck:

2.0 Conventional Fuels, 2.1.2 Effects Assessment, 2.1.2.1 Human Health Effects, Pg. 2-15, line 29 and 2-16, line 1: Why is the term "aerosolized" used when the gasoline, even if it was prayed as an aerosol, will vaporize immediately because of its high vapor pressure? "Vaporized" is probably the more correct word choice.

Winner:

2.1 Risk Assessment Research Framework: The Research Plan shows that the document, and the research program currently in place, lack sufficient integration at several levels. Integration appears to be lacking within existing research teams. For example, the fate and transport teams have not conveyed research results to the ecosystem scientists. Increased interaction between the EPA research groups involved in the Alternate Fuels Program would improve efficiency of the overall effort.

The EPA Alternative Fuels Program appears to be proceeding in isolation. Although parallel programs were acknowledged in the EPA, the DOE and DOT, little effort has been developed to integrate work between these agencies, or state and city agencies where alternative fuel use is expected to increase. The Research Plan does not clearly identify participants and their probable roles.

Miller:

2.1.2 Effects Assessment, 2.1.2.1 Human Health Effects, Pg. 2-16, lines 17-21: Resolution of whether gasoline meets the criterion for a2u should receive a high priority, since much data are available and the potential impact on additional research is great. Also, additional research has been conducted on hepatocyte cell proliferation in mice following exposure to unleaded gasoline vapors (Tibury et al., J. Toxicol. Environ. Hlth. 38:293-307, 1993) showing the importance of this endpoint in understanding the sex-specific hepatocarcinogenic response of this complex mixture.

Schreck:

Pg. 2-17, line 7: This sentence points to the fact that some data exists on the health effects of leaded gasoline fuel exhaust, but little material exists for unleaded fuels. Rather than combining the two fuels as suggested in this sentence, they should be treated as different materials for the purpose of this study. Leaded gasoline

exhaust contains a fine lead aerosol along with various PAH compounds which can not be used in the presence of lead. In contrast, unleaded gasoline engine exhaust has no lead and is catalytically treated to burn off many of the PAH compounds produced during primary combustion.

The need is quite apparent that realistic exhaust from the combustion of unleaded fuels in modern engine/catalyst power plants has not been studied for health effects and that this major 'benchmark' against which all alternatives to the current system need to be evaluated remains to be determined. Therefore, I fully support the closing paragraph of this section that testing of the current unleaded fuels needs to be done along with determination of health effects by contemporary evaluation techniques.

Mauderly:

Pg. 2-17, lines 9-12: The statement is confusing. Is the intent to suggest that IARC came to the wrong conclusion? Perhaps the author means that some studies provide evidence "suggesting that gasoline exhaust may be carcinogenic."

Wood

2.1.2 Effects Assessment, 2.1.2.1 Human Health Effects, Pg. 2-17, lines 19-30: The running wheel studies, Murphy etc., reviewed in HEI chapter, provide a good strategic lead for this problem.

Suter:

2.1.2.2.1 Terrestrial Ecosystem Effects, Pg. 2-18: Calls for microcosm/mesocosm studies of terrestrial ecological effects. Which of the effects discussed are best studied in the sort of test system, and are they the most important terrestrial ecological risks? In other words, how did this come to be your research recommendation?

Suter:

2.1.2.2.2 Aquatic Ecosystem Effects, Pg. 2-18: Calls for mesocosm studies. Before these are planned, thought needs to be devoted to how the results will be

extrapolated to the field and whether useful insight will be obtained. If you add significant amounts of a petroleum product to a typical pond mesocosm, you know in advance that it will go anoxic. Given that there is little tanker or barge traffic on farm ponds, what do the anoxia and subsequent ecosystem responses tell you about the extent of anoxia and subsequent response in the actual exposed systems? Certainly the processes of ecological recovery are not the same in those systems. Community-level effects are ecosystem specific. You might do better to model the processes in rivers and estuaries on the basis of laboratory studies of processes than to try to extrapolate from a pond mesocosm. The abandonment of mesocosms by the Office of Pesticide Programs should tell you something about your agency's ability to use and interpret data from those tests.

Winner:

2.2 Background and Rationale: Research is prioritized for conventional fuels and for the four basic types of alternative fuels. Little rationale is presented for distinguishing high priority work from work of less priority. Stated another way, the research goals are not specific, but overly general and fuzzy with no focus or endpoints. In addition, I am not sure that top priority is given to topics of greatest importance. For example, testing the capacity for existing fuel storage tanks and piping to handle alternative fuels, and defining the most seems more important that fate and transport studies, or many other topics given a priority rating of 1.

Pefley:

Figure 2-4. Emissions versus air/fuel ratio, Pg. 2-28: The figure should be presented using normalized air/fuel ratios. In normalized form the emissions profiles for the various fuels are easily comparable.

Mauderly:

Pg. 2-46: This entire section needs to be examined to ensure that the species (strain when possible) and exposure pattern are given for the studies that are discussed. There are numerous places where this is a problem, and I will not attempt to point out each one individually. It is of no use to the reader, for example, to learn on Pg. 2-49, line 8, that effects begin at 40-50 ppm benzene, unless that exposure is put into some kind of context. Nowhere in the paragraph do we learn if these studies

used continuous or single exposures, or something in between. In line 22 of the same page, for example, what strain of mice were used? This problem becomes particularly intense on page 2-54 and later. In addition, the word, 'Beagle' should be capitalized. In general, the section needs substantial editing. References to studies just aren't useful to the reader unless these details are given. Furthermore, their exclusion discredits the report by suggesting that these details were not considered in synthesizing the information.

Mauderly:

Pg. 2-46, lines 13-14: While the statement is generally true, it should be recognized that we still don't know how the carcinogenicity of diesel exhaust in rats might be related, if at all, to potential carcinogenicity in humans.

Schreck:

Pg. 2-47, Table 2-6: Motor Vehicle Emissions Risk Estimates, Cancer Incidences Per Year: Entry 6 lists "gasoline particles," ... does this mean the lead aerosol from leaded fuel exhaust?

Miller:

P. 2-47: This discussion of butadiene carcinogenicity should be expanded to include recent work (Csanady et al., Carcinogens 13:1143-1153, 1992) that demonstrates significant metabolic differences between mouse, rat, and human microsomes for butadiene. In addition, the carcinogenicity results from butadiene suggested from animal studies indicate an increase of hemangiosarcoma of the heart. Since this is a relatively rare tumor, consideration should be given to epidemiological investigation of death certificates from a national survey to determine if there is any association between butadiene exposure in man and hemangiosarcome of the heart. A number of modeling efforts have been published since 1989. The document should be modified to reflect work on mechanisms, exposure rate, adduct formation, and human dosimetry covered in these papers (Bois et al., Toxicol. Letters 56:283-298, 1991; Bois et al., Toxicol. Appl. Pharmacol. 110:79-88, 1991; Boi, F.Y. and Paxman, D.G., Reg. Tox. and Pharmacol. 15:122-136, 1992; Travis et al., Toxicol. Appl. Pharmacol. 102:400-420, 1990; Travis et al, Atmospheric Environ. Vol. 25A, No.8, 1643-1647, 1991; Sun et al., Fundam. Appl. Toxicol. 15:468-475, 1990).

Shreck:

Pg. 3-94, line 17: "Do not believe PM (particulate matter) issues from M85 vehicle exhaust, although M100 diesel vehicles do produce a fine carbonaceous aerosol."

Schreck:

3.3.2 Effects Assessment, 3.3.2.1 Human Health Effects, 3.3.2.1.2 Primary Fuel--Methanol, Pg. 3-96, line 6: "The point about coexposure to gasoline and methanol with M85 is a good one and brings to mind that co-metabolism of the two should also be considered. Furthermore, dermal studies have shown that the two are cosolvents and accelerate the penetration of M85 into the body through the dermal route. This raises the issue that M85 dermal toxicity may be greater than anticipated by studying the dermal uptake of either of its constituents."

Miller:

3.3.2 Effects Assessment, 3.3.2.1 Human Health Effects, 3.3.2.1.2 Primary Fuel--Methanol, Pg. 3-96, lines 20-23: Research on M100 and M85, as well as gasoline, are advocated in the document research strategy. However, as noted earlier, the penetration of M100 into the market would indicate the M85 should be given a higher priority for research compared to M100.

Schreck:

Page 3-97, line 6: "Even if neurotoxic effects are not found to be a major problem at low levels of exposure, this paragraph covers, in an understated manner, some important and fundamental items which need to be learned about methanol metabolism and resultant toxicity. The effect of format on the tissues of the nervous system is the most obvious but its effect on tissues throughout the body may be of equal or greater importance in explaining the broad range of toxic phenomenon attributes to methanol. Only with this knowledge can animal models be chosen for study with confidence that they model the toxic reactions we wish to study in humans."

Wood:

3.3.2.1.3 Combustion and Atmospheric Transformation Products, Pg. 3-98 and 99: Airborne irritants are responsible for much of the misery and reduction in the quality of life associated with automotive emissions and photochemical transformation products. I would encourage focused attention on irritation. Eye irritation deserves separate evaluate studies, and the techniques were reviewed in the last chapter of the HEI book. (4-39 I think there is more data on PAN eye irritation than is cited here.)

Mauderly:

3.3.2.1.3 Combustion and Atmospheric Transformation Products, Pg. 3-99, lines 20-22: Here, and elsewhere on the page, the issue of the relevance of *in vitro* mutagenicity to human carcinogenicity is raised. This particular statement indicates that comparative potency and bioassay-directed fractionation have proved valuable for assessing risk from combustion products. If that is the intent, then what is the example that makes the case? Perhaps the best example of an attempt to do this is diesel exhaust; however, this example does not make the case. Indeed, current EPA risk estimates for diesel exhaust specifically exclude consideration of the soot-associated organics, which were the sole focus of the comparative potency and bioassay-directed fractionation efforts. Once can argue that mutagenicity ought to be related to cancer risk, but if there are examples proving this to be established for combustion mixtures, then they should be given.

Miller:

3.3.2.1.3 Combustion and Atmospheric Transformation Products, Pg. 3-100, lines 1-3: This reviewer would reemphasize that careful consideration of any field monitoring correlated with epidemiological assessments is needed. The probability of such studies contributing significant information for risk assessment is unlikely and, therefore, such studies should receive a low priority in the research strategy.

Miller:

3.3.2.1.4 Research Objectives, Pt. 3-101, line 26: Insert the word "for" for the word "conventional".

Miller:

3.3.2.1.4 Research Objectives, Pg. 3-102, line 4: To this reviewer, the rationale for studies on the potential for long term respiratory impairment with recurrent acute exposures has not been adequately established. Moreover, a priority level of one appears unwarranted, especially since the TLV for this compound is based upon irritancy and exposure levels that would not be anticipated to be anywhere near those used to set TLVs.

Miller:

3.3.2.1.4 Research Objectives, Pg. 102, line 9: The research strategy prioritization scheme that uses only a priority one and a priority two does not appear to provide enough delineation of potential merits of various components of the research. For example, the chronic bioassays are given a priority level of two yet they are acknowledged to be dependent upon the results of a number of studies which have a priority level of one for a number of years. This reviewer would suggest that EPA provide up front a discussion of the implications of their prioritization scheme relative to levels and years of proposed funding.

Suter:

3.3.2.2.3 Marine Effects, Pg. 3-105, line 27: The aquatic ecosystem research priorities for the alternative fuels are basically the same as for conventional fuels. (In fact there has been some careless use of text copy functions as in the reference to gasoline in the methanol section. The general problem that I see in these sections seems to result from the idea that after a preliminary assessment one research project leads to another rather than iteration of assessment-research-assessment-research...(e.g., pg. 3-102, lines 19-102 versus Fig. 1-4).

The question of whether to emphasize acute toxicity testing for spills or chronic testing for continuous releases can be resolved by abandoning the conventional test dichotomy. The critical issue is how rapidly are effects induced or a kinetic equilibrium induced in the most sensitive life stages. Therefore, if you are concerned about effects of spills on fish, you would develop a concentration-duration-response function for the material in exposures of larval fish rather than generating a 96-h LC50.

Schreck:

4.0 Ethanol, 4.2.2 Effects Assessment, 4.2.2.1 Human Health Effects, 4.2.2.1.1 Ethanol, Pg. 4-29, line 28: "Dermal absorption of ethanol is insignificant, but has anyone checked the cosolvency of ethanol-gasoline mixtures? It may also be true that gasoline accelerates the dermal penetration of this alcohol."

Miller:

4.2.2.1.1 Ethanol, Pg. 4-33, lines 7-9: The study of Pequignot and Tuyns (1980) is cited as showing moderate intake of ethanol to be associated with increased risk for developing cirrhosis, but no definition of "moderate intake" is provided. In view of the earlier discussions on route-to-route extrapolation between oral inhalation, it would be worth providing this definition.

Mauderly:

4.2.2.1.2 Acetaldehyde, Pg. 4-36, line 8: What does "intermittent" mean? This is not useful without clarification.

Mauderley:

4.2.2.1.2 Acetaldehyde, Pg. 4-36, line 20: Are these Syrian hamsters? "Hamsters" are define in line 29 - be consistent.

Miller:

4.2.2.1.2 Acetaldehyde, Pg. 4-38, lines 10-19: The discussion of the RfC for acetaldehyde implied a factor of 10 to the fourth power as being used for a number of uncertainty factors present in the data. The resultant 0.009 ug/m3 seems suspect, since this reviewer is under the impression that no greater than 10 to the third power is used by EPA for uncertainty factors. While the statement is made that the confidence in the RfC is low, the Research Strategy document should put a high priority on research that would eliminate some of the uncertainty factors in this calculation.

Mauderly:

4.2.2.1.2 Acetaldehyde, Pg. 4-39, lines 5 and 6: This is a confusing sentence; "hyperplasia" is "cell proliferation".

Mauderly:

4.2.2.1.3 Peroxyacetyl Nitrate, Pg. 4-39, line 14: The order of magnitude of ambient concentrations should be given for context.

Miller:

4.3.2.1.4 Research Objectives, Pg. 4-57, line 16: Insert the word "for" before the word "conventional".

Schreck:

5.0 Compressed Natural Gas, 5.2.2 Effects Assessment, 5.2.2.1 Human Health Effects, Pg. 5-17, line 11: "The discussion of the simple asphyxiant properties of methane does not take into account the 10-15% non-methane content of CNG. Recent work has claimed that the simple aliphatics methane, ethane and propane may be fast acting anesthetics rather than simple asphyxiants."

Mauderly:

5.0 Compressed Natural Gas, 5.2.2 Effects Assessment, 5.2.2.1 Human Health Effects, Pg. 5-17, lines 14-17: How can you reconcile the fact that methane is rapidly absorbed and readily metabolized, with the fact that most methane is exhaled unchanged? Is the exhaled methane the fraction that was never absorbed in the first place? If so, they why wouldn't it be unchanged?

Colome:

5.1.1 Exposure Assessment, 5.1.1.1 Source Characterization, 5.1.1.1.1 Emissions from Feedstock and Fuel Production, Storage, and Distribution, Pg. 5-2, line 10: As I understand it, the current supply of methane is adequate well into the next century. This line states that CNG might be derived from coal in the "near future." Please be more specific and define the near future in terms of dates when the conversation is likely to be economically and technically feasible.

Colome:

5.1.1 Exposure Assessment, 5.1.1.1 Source Characterization, 5.1.1.1.1 Production, Pg. 5-2, lines 14-23: This section recommends a hazard assessment

study for accidental releases. However, a considerable amount of information already exists on the safety and hazards of this fuel. DOE and industry information should be reviewed before additional studies are undertaken.

Colome:

5.1.1.3 Exposures, 5.1.1.3.1 Human Exposure Assessment, Pg. 5-6, lines 5-14: Asphyxiant risk should be relatively low since, unlike propane which sinks into low pockets by gravity, methane mixes with ambient air and dissipates relatively quickly. Therefore, even when significant emissions occur, the concentrations will be lower than for propane.

Colome:

5.1.1.4 Analytical Methodology, Pg. 5-7, lines 20-25: The document recommends development of improved NO2 monitors due to interferences that have been detected from nitric and nitrous acid using current measurement methods. This may not be necessary if the interfering acid species are co-linear with NO2. It may also be preferable to measure the acids directly and subtract their contribution to the NO2 monitor after studying their interference characteristics.

Colome:

5.3 Research Needs, Pg. 5-19, line 5: This sentence suggests that natural gas is abundant worldwide. My reading of the data agrees with this conclusion but the statement is not consistent with the comment made on page 5-2, line 10 of the document.

Colome:

5.3.1.3 Exposures, 5.3.1.3.1 Human Exposures, Research Objectives, Pg. 5-23, lines 13 and 14: Any exposure model developed should be general and does not need to be specific to CNG. The specific physical characteristics of CNG would be inputs to the model but it is best to think in terms of physical models that are based upon first principals and add submodel features only as necessary.

Colome:

5.3.1.4 Analytical Methodology, Pg. 5-24, lines 4-5: The statement on the need for NO2 monitors is repeated.

Schreck:

5.3.2 Effects Assessment, 5.3.2.1 Human Health Effects, Pg. 5-25, line 8: CNG does appear to be so clean burning that it poses few challenges for health effects study. However, CNG poses physical dangers to users which should not be ignored in assessing its health risks. The fire hazard is always present with hydrocarbon fuels, but a gaseous fuel in any still air environment is a special additional risk. Also, the compressed gas has a large amount of potential energy which could be released in an accident with dangerous consequences.

Mauderly:

5.3.2 Effects Assessment, 5.3.2.1 Human Health Effects, Pg. 5-25, line 16: Would the intent be to have concern for the carcinogenic and toxic potentials only at relevant exposure concentrations? The "potential" for toxicity will certainly exist otherwise.

Mauderly:

5.3.2 Effects Assessment, 5.3.2.1 Human Health Effects, Pg. 5-25, line 20: Would this be a bioassay of CNG, or its combustion products? The intent isn't clear.

Schreck:

6.0 Reformulated Gasolines, 6.1.2 Effects Assessment, 6.1.2.1 Human Health Effects, Pg. 6-11, line 22: Discussions of the health effects of reformulated gasoline bring the questions of health effects of unleaded gasoline back into discussion and reemphasize the need for these studies. Beyond that, the MTBE and ETBE health studies need to be completed and viewed alongside the gasoline results.

Mauderly:

6.1.2 Effects Assessment, 6.1.2.1 Human Health Effects, Pg. 6-12, lines 5 and 6: It is interesting that the lung is not listed as a potential target organ. Is this because there are no human data on inhalation of MBTE, or because the existing data lend confidence that the lung would not be a target from inhaled MBTE?

Mauderly:

6.1.2 Effects Assessment, 6.1.2.1 Human Health Effects, Pg. 6-12, line 11: If the chronic study "is due" to be finished in 1992, there should be an update of at least preliminary information by now.

Mauderly:

6.1.2 Effects Assessment, 6.1.2.1 Human Health Effects, Pg. 6-12, line 12: Concentrations are subsequently listed in ppm, so why not here?

Wood:

6.1.2 Effects Assessment, 6.1.2.1 Human Health Effects, Pg. 6-12, lines 15-24: The description is in error, compare to tables 22, 23 of original studies. Female brain width was affected at 8000 ppm, nonselectively. Male brain length was selectively affected at 4000 ppm, nonselectively at 8000.

Schreck:

Pg. 6-12, lines 3-24: MTBE's use in humans and the EPA Reference Concentration of 0.5 mg/m3 all provide confidence that exposures incidental to reformulated gasoline handling will be safe.

Schreck:

Pg. 6-13, line 12: The lack of any information about the health effects of ETBE is worrisome and the proposed standard toxicity testing is to be recommended if this ether will be used in larger amounts.

Mauderly:

6.2.2 Effects Assessment, 6.2 2.1 Human Health Effects, Pg. 6-30, lines 23 and 24: Aren't the "Department of Energy" and the "National Laboratories" redundant?

Mauderly:

6.2.2 Effects Assessment, 6.2.2.1 Human Health Effects, Pg. 6-30, lines 26-29: It is true that different fuels and operating conditions can alter the ratios of mutagens in diesel soot extract, but it is also true that chronic studies have shown that exposure-response relationships for lung cancer do not differ much among studies using different engines, fuels, and operating conditions. The implication of the sentence is that health outcomes might differ according to these variables, but there is little, if any, experimental support for this. Diesel exhaust is a poor example to use for the fact that these variables, which affect mutagenicity, also affect health outcomes.

Mauderly:

6.2.2.1.1 Methyl-Tertiary-Butyl Ether, Pg. 6-31, line 19: Consistency in designating strains is desirable. Elsewhere in the document, "F344" is used.

Schreck:

6.2.2 Effects Assessment, 6.2.2.1 Human Health Effects, 6.2.2.1.1 Methyl-Tertiary-Butyl Ether, Pg. 6-31, line 23: MTBE absorption dermally was not significant as a pure compound, however it should also be tested for skin penetration when mixed with gasoline.

Mauderly:

6.2.2.1.1 Methyl-Tertiary-Butyl Ether, Pg. 6-33, lines 1-10: It is of questionable usefulness to describe studies that you then determine are not useful.

Mauderly:

6.3.2 Effects Assessment, 6.3.2.1 Human Health Effects, Pg. 6-50, line 22: The common abbreviation "TSCA" should be used and defined in the list of abbreviations.

Schreck:

6.3.2 Effects Assessment, 6.3.2.1 Human Health Effects, Pg. 6-51, Research Objectives: Add a fifth objective. In view of the possibility that reformulated gasoline will be used by the public as it does gasoline for a solvent for washing parts, etc. and because gasoline mixed with some hydrocarbons may potentiate their dermal penetration, dermal penetration studies should be conducted with both MTBE and ETBE in gasoline over a range of mixture concentrations.

Wood:

6.3.2 Effects Assessment, 6.3.2.1 Human Health Effects, Pg. 6-51, lines 2-3: There must be more hazard identification with MTBE. Pharmacokinetics come second.

Schreck:

7.0 Scientific Assessments, Scientific Assessment Objective, Pg. 7-3, lines 1-15: I agree with the priorities attached to Objectives 1 and 2. Communicating this information (Objectives 3 and 4) also seems to be important and prioritized to reflect this.

General Comments:

Schreck:

General Comments: This strategy generally benchmarks alternative fuels against gasoline. This is probably the most workable and understandable approach since the public is familiar with the risks of using gasoline as a transportation fuel. However, not only is the public not necessarily well informed about the actual health risks of using gasoline, the scientific community is going to have to be careful working with existing data. In particular,\ gasoline engine exhaust health studies performed

with leaded fuels are likely of little value and may mislead researchers about modern exhaust emissions. Fuel vapor studies of unleaded gasoline or reformulated gasolines will have to be done carefully to replicate the actual exposures from fuel funds, rather than simply the vaporized fuel. Atmospheric transformation of emission products from each of these possible fuels makes the study even more complex - indicating that EPA should proceed cautiously in committing resources to any one portion of this strategy until the commercial viability of the fuel is determined.

My general impression is that the document EPA/600/AP-92/002 entitled "Alternative Fuels Research Strategy," is a well structured outline for investigating the health and ecological effects of the range of alternative fuels currently being considered in America for automotive use. Realistically, the change to new motor fuels will probably be gradual, since economics, distribution systems and technology all tend to slow novel systems from entering the market place until they establish a niche. Therefore, EPA doesn't have to understand all things about all prospective fuels at the onset of their consideration for use. This is fortunate since the available budget discussed in "Issue Plan Number 17" will not support a highly ambitious research program on all fronts. It appears then, that the real strategy will be to assign resources to portions of the "Strategy" which are pivotal to understanding the possible health implications of those fuels which have both a credible scenario for exposure with toxicity and a viable chance of actually reaching the marketplace.

Methyl-tertiary-butyl ether (MTBE): MTBE and its cousin ethyl-tertiary-butyl ether (ETBE) are already in use in the production of reformulated gasolines and millions of people are currently exposed to them by inhalation and dermal contact. It is therefore highly appropriate that EPA has taken the initiative and designed and implemented a human exposure study (as directed by Dr. Gerrity at the meeting). This research will help to answer immediate questions concerning purported health effects and, if the additive is shown to be safe, assure its continued presence in the marketplace.

Methanol and M85: Since methanol and M85 are the next most viable alternative fuels for toxicity study based on the current economic interest, number of new vehicles in use and credible toxicity scenario, it was also good to note that EPA

has begun testing methanol not only against teratology endpoints but also in metabolism studies. This metabolic work is fundamental to understanding mechanisms and to interpreting whether any animal models of methanol's toxic effects have actual applicability to humans. Again this work is of strategic importance to the health effects program because it is pivotal to justifying any planned future work. Human exposure studies needs its findings to establish the range of exposures as toxic metabolites begin to accumulate in the body and might begin to cause subtle effects in chronic rather than acute toxicity studies. Currently any animal studies of methanol's toxicity are suspect because the metabolism of methanol is different in humans than in non-primates and even primates seem less affected by methanol, judging by differences in toxic doses. EPA's human studies may justify animal models of methanol toxicity by showing what pharmacokinetic parameters have to be matched between man and an animal model to have a valid test.

Emissions Characterization and Air Quality: In addition to the importance of the two above mentioned items, the measurement of emissions from the tailpipe and in refueling scenarios appears to be the portion of the program outline which needs to be funded 'up front' in order to determine which elements of the research outline warrant funding. It therefore seems logical to use limited resources first in this area with priority given to measuring exposures and dosimetry. From this, risk analyses, ranges of exposure for toxicity studies, etc. can all be determined for future analysis and prioritization of research projects.

Mauderly:

In general, the health effects sections of the report are in reasonable shape, and require only modest editing. The section on Conventional Fuels is in need of the most editing.

There are general needs for editing that apply throughout the sections. Care must be taken to give uniform treatment to the description of studies. It is not useful to list exposure concentrations, for example, unless the exposure pattern is also given. In a few cases, studies are referenced only to be discounted for some reason. First, only studies thought worthy of consideration should be included at all. Second, if a

study is worth including, it is worth describing in sufficient detail that the reader can understand its basic design. A similar problem relates to the description of animals. At a minimum, the strain and gender should be given, and designations of strains should be uniform throughout the document.

Another general issue is the repeated emphasis on the use of *in vitro* mutagenicity testing to compare potentially toxic materials. In several cases, the example of diesel exhaust is either stated or implied. At this point, it is known that the mutagenic organic fraction of diesel soot apparently does not contribute significantly to its carcinogenesis in rats. Indeed, EPA's current risk assessments specifically exclude this fraction in dose equivalence extrapolations. Mutagenicity might be a good signal for carcinogenicity for some materials, but is certainly not a good signal for others. Much of the present draft appears written in ignorance of this issue, which has been generally known in the field for a couple of years.

A third general issue relates to the uneven treatment of references to the laboratories producing the data described. Some sections take on the flavor of "commercials" for certain research groups, while other laboratories producing referenced data are not mentioned at all. This is not a "show stopper"; indeed, there may be a very good reason to mention institutions at some point. The basis for doing so is not apparent, however, and some attention needs to be given to the uniformity of treatment of this issue across the document.

Finally, the treatment of research needs should be given additional thought. In some cases, the "Risk Assessment Research Framework" and "Background and Rationale" sections contain descriptions of research needs, while in others, these needs are confined to the "Research Needs" section. It is a bit confusing, and not very efficient, to find research needs described in two or three places.

Considering the above comments, the document seems to be generally on the right track in pointing out overall key research needs, and that is its major purpose.

Goldstein:

Although I have some major criticisms with respect to the document, I wish to compliment the authors on an excellent attempt to lay out a strategy for a very broadly scoped and complicated issue. I am very impressed with the clear writing, the integration and cross referencing among chapters and the ability to select strategic research priorities.

The most significant shortcoming with the document is that it lacks a concise and complete integration of the research strategy. Priorities regarding different aspects of the program are scattered throughout the document. Nowhere are these priorities assembled in a concise form that defines their interrelationship. Neither the executive summary, nor the introduction (which is more an extended summary than an introduction) includes all the priorities and key decisions (e.g., the selection of the South Coast Air Basin) that compose the strategy. On the other hand, from an editorial perspective, the document is extremely repetitive. Its size could be reduced by at least 50% without losing any information.

P.S.C. Rao: (Was invited to attend the meeting as a consultant, but declined; however sent written comments to Dr. Judy Graham re Ecosystem Section).

I found most of the major research issues on the direct impacts to be adequately covered. That is, research needs for understanding transport and transformations of alternate fuels and their constituents in soils, groundwater, and aquatic systems are addressed. Indirect effects of catastrophic releases of methanol- and ethanol-based alternate fuels, are, however, not dealt with as well. Assuming that aquatic sediments (both freshwater and marine) that might be subjected to such large-volume releases of alternative fuels are already contaminated with various hydrophobic organic chemicals (e.g., PCBs, dioxins, DDT, PAHs), the ecological impacts of high levels of ethanol and methanol on release of such organic contaminants must be better understood. The long-term impacts on aquatic systems of release and redistribution of these low-solubility, high-toxicity contaminants might be much more serious than the short-term, acute impacts (e.g., fish kills from DO depletion, methanol/ethanol toxicity). I suggest that this issue be given stronger consideration in judging the ecosystem effects of alternate fuels. I believe that these types of impacts are much

more important in aquatic systems, compared to terrestrial systems (including groundwater).

Utell:

Major Comments: Overall the health sections of the document are well written. The major problem identified was the absence of detail regarding anticipated exposure levels and health effects identified in the animal toxicologic studies. For example, in the majority of the health sections, there is a discussion on cancer as an endpoint often utilizing extraordinarily high doses of toxicants in animal inhalation studies. I would strongly urge the authors to develop a table for each of the potential alternative fuels that provides a best estimate of realistic ambient concentrations, potential exposure scenarios, and the range of doses used in animal studies resulting in a health effect. This would place the health effects data in a more realistic setting.

In addition, the potential contribution of the identified toxicants from other exposure routes should be included. For example, the dose of methanol that results from drinking a couple of diet Cokes is impressive. It is particularly relevant that some efforts have been made to characterize methanol body burdens for inhalation exposures under high exposure scenarios in terms of added body burdens of methanol resulting from ingestion of two 12-ounce diet beverages. Again, such data bring clinical relevance to a very diffuse literature.

Specific Comment: Throughout the document, the reference to CIIT as a partner in research effort is troublesome. No other research institution is referred to by name. In all other cases, the work is attributed to the investigator rather than a specific institute. It was not clear to me whether the EPA or CIIT was writing sections of this document. Frankly, I found the selection of one Institute offensive. This should be modified!

Winner:

The Research Strategy is an important document because alternative fuels will become increasingly important especially in urban areas currently out of compliance

for 03 and CO standards. The switch from conventional to alternative fuels will bring significant changes in atmospheric chemistry. Decreases in 03 and CO levels are likely and are worthy goals. However, increased use of alternative fuels will bring many uncertainties in all phases of fuel production and use.

EPA staff and associated scientists are to be commended for their efforts at organizing a large amount of information into a single volume. The Research Plan shows much of that which is known and does a convincing job of highlighting that which is not known. Opportunities to improve the Research Plan exist and include:

Develop site analyses for each of the nine urban areas likely to switch to alternative fuels. Data bases on fuel use patterns, changes in fuel use anticipated from the Clean Air Act, should be developed for each critical urban area. A GIS system should be developed that shows current and projected air pollution inventories, human and ecosystem resources at risk, and calculated estimates across the region of costs and benefits due to different air pollution scenarios. Initially these nine site analyses would be crude, but a goal of research efforts would be to refine the GIS capability at each site. Such site specific analysis may be necessary because patterns of fuel use, the chemistry of optimal alternative fuels, and impacts of air pollutants may be unique at each urban area currently out of compliance. Site specific analysis, done with consistent approaches, will allow comparisons between sites, but allow for optimal resource management within sites.

The document could be reorganized and shortened by 50% without loss of content. Such shortening would make the Research Plan more readable. Efforts to edit, improve syntax, and eliminate redundancies would be helpful.

Presentation of an estimated budget and FTE requirement would help reveal the scale of the proposed research.

Suter:

The EPA is to be commended for taking a risk-based approach to this research strategy. As I stated during the workshop that kicked-off this program, the purpose of this research must be to support risk assessments by reducing uncertainty in the risk estimates. However, there are still no risk assessments or even a risk assessment framework for alternative fuels. Therefore, the issues raised in this strategy are based on expert judgment which is simply fit into components of the risk assessment process. As I stated previously, and as a number of reviewers said during the CASAC meeting, you can only be reasonably certain that you have identified the significant issues for risk assessment if you have designed and preliminarily implemented the health and ecological risk assessments. An additional advantage of doing risk assessments as early in the process as possible is that you may be able to reach some conclusions about relative risks that will be useful to government and industry decision makers.

The comment above is not meant to imply that the strategy should be held up until risk assessments can be performed and incorporated. Rather, the EPA should move forward and begin to implement the scheme presented in Figure 1-4.

The current strategy tacitly assumes that there are acceptable existing methods for comparative risk assessment of motor fuels. Particularly for ecological risk assessment, that is not the case. The comparative ecological risk assessment performed by Cooper et al. for the SAB points out the need for research to develop formal ecorisk methods. The best way to do this would be to develop a comparative ecological risk assessment framework for motor fuels, implement it as far as possible, and then perform the research necessary to fully implement it. You will note that this is in effect a subset of the previous comment; the difference is that no class of research needs is added, development of risk assessment tools and procedures. Without such research the program could find itself with data and a mandate to guide decisions and no way to connect the two. The major criticism of NAPAP was that it put itself in that position. This program should learn from NAPAP's experience.

If the EPA is to be the agency responsible for performing comparative risk assessment, then the risk assessment must include the full range of issues. For

example, the DOE and USDA are performing research on the environmental effects of biological feedstock production that would be input to an integrated assessment, but the EPA must develop risk assessment methods that allow those effects to be balanced against ecotoxic effects.

If the EPA performs the integrated health and ecological risk assessments for alternative fuels, those assessments could serve as a tool for involving the other agencies and private parties in the research program. That is, if issues that are of interest to other parties are shown to constitute major sources of uncertainty in a risk assessment or if a preliminary assessment suggests a major risk that may be resolved by additional research, those findings would constitute inducements to perform the suggested research.

Given the small budget for this program relative to the magnitude of the problem, and given the fact that even with risk assessment results to help prioritize issues, there are strategic decisions that must be made about research prioritization, the EPA should lay out a logic or set of decision rules for narrowing the list of issues for research.

The following rules are presented as examples:

a. Emphasize fuels that are most likely to be used in volume in the near term.

b. Investigate those risks that are potential show-stoppers.

c. Perform research that could eliminate major issues from further consideration.

d. Perform research that is relevant to multiple health and ecological endpoints (e.g., source characterization and atmospheric chemistry).

Some of these rules have clearly been adopted by the EPA, but I did not see them laid out clearly in one place.

Jeffries:

The general approach to the "Alternative Fuels Plan" as outlined on page 1-25 of the Review Draft of Alternative Fuels Research Strategy is excellent. This section states that the primary focus of atmospheric studies needs to be characterizing the impact of alternative fuel use on ozone formation in urban and rural areas. The last two sentences on the bottom of this page set up expectations for what an atmospheric fate program ought to look like. Unfortunately, the remaining chapters do not follow through on this vision. In fact, we were told that this part of the program will be cut in the future. This undermines the health effects work that is so prominent in the plan.

EPA does not know if its regulatory photochemical reaction mechanism, used to determine atmospheric fate of vehicle emissions, is biased with regard to the predictions of benefits of changes to use alternative fuels. This is because there has not been any in-house work nor AREAL-sponsored external work on this subject. One reason this has not happened is that reliable environmental chamber data to carry out such evaluations are limited. Nevertheless, some evaluations are possible and these have not been done. Such studies are strongly recommended. EPA also has not produced the chamber data needed to conduct compelling evaluations in the future. While it is true that CRC has funded some work on M85, this has stopped. DOE is funding some work which may examine E85. Chamber data for CNG and LPG do not exist. There is now an EPA evaluation protocol for reaction mechanisms which was completed in the last year and this should be examined as to how it would be applied to the problem of predicting air fate with regard to alternative fuels.

In the CRC alternative fuels program, when the current EPA reaction mechanism Carbon Bond Four (CB4), used in the Urban Air Shed model, was compared with the smog chamber data for urban VOC with Industry Average Gasoline (IAG) emissions and urban VOC with M85 emissions, the results revealed a systematic positive bias for ozone predictions of nearly 50% and furthermore showed that CB4 overestimated the benefits of M85 relative to IAG by approximately 30% (Jeffries, et al. CRC Final Report on ME-1, 1993). A similar result was obtained for the Carter reaction mechanism used in the California alternative fuels modeling work. Such results seriously weaken arguments for the use of M85 based on ozone reduction benefits of M85 that have been demonstrated by modeling studies.

It is a false assumption that current oxidant models can adequately predict the secondary pollutant effects of large scale compositional changes due to use of alternative fuels.

ORD researchers have never performed in-house air shed simulations to evaluate scenarios intended to examine benefits of changes to alternative fuel. Thus, they have no first-hand knowledge of weakness, problems, and uncertainties in the external studies which have been performed and they have little basis for critical review, nor the ability to detect critical assumptions, and to plan research to address these.

Many comments on the alternative fuel's benefits in the Plan carry the hidden assumption that "reactivity" is in the fuel emissions. In this case, the "Air Fate" sections (e.g., page 1-25) do make clear that our "advanced understanding of O3 formation" reveals that the species itself comprises only part of the origins of reactivity, the other part being the environment in which the fuel emissions are reacting. The rest of the document, however, continues to rely on the hidden assumption above. I believe that this problem is due in part to not having done any of the atmospheric fate work at EPA. There is also a tendency to believe that low specific reactivity is an adequate reason for believing that alternative fuels will provide atmospheric benefits, for example, lower ozone concentrations. This ignores the effect of mass compensation on low specific reactivity. For example, both trajectory and advanced grid models using different photochemical reactions mechanisms, show that in urban areas, more than one-half of the ozone formation is due to reactions of CO, methane, and the aliphatics, and the "most reactive" species contribute less than 20% in total. This is mostly due to the abundance of CO, methane, and the alkanes in urban air and the fact that urban air tends to be "radical rich." Thus, essentially all carbon contributes to the production of peroxy radicals that are needed to oxidize NO to NO2.

Wood:

There was general agreement that a comparative risk assessment strategy is an appropriate approach to setting research priorities for alternative fuels . With this model, research attention is focused on known risks of exposure, and seeks to enhance knowledge critical to the risk assessment. This presumes of course that we

know what the hazards are; unfortunately, we don't. Thus we are guilty of "looking for the keys around the lamp post, because that's where the light is..."

Thus, I would urge effort in hazard identification. This is certainly true for neurobehavioral toxicity of MTBE. More generally, I would encourage mechanistic investigations when possible, because they may alter risk assessment methodologies. This is particularly true for methanol, where the issues of systemic acidosis vs. target xenobiotic activation have yet to be elucidated.

Dr. McClellan suggested using conventional fuels as a standard of comparison, and then undertaking the study of alternatives in comparison. This is a reasonable approach if a standard mixture can be specified. However, I think there is much to be gained by studying less complex mixtures, and pure chemicals, in an attempt to identify bad actors within the complex mixture. This would help to provide the necessary information to guide attempts to reformulate not just fuels, but also to guide the regulation of exposure to these compounds in other societal contexts, be they indoor air pollutants, consumer product utilization, the workplace and the outdoor environment.

The guiding principle is to minimize harm. If a mixture can be changed to eliminate a toxic component or an eventual emission product, then there should be some assurance that the result will in fact be an improvement. Thus, putting in an agent with unknown toxicity may be foolhardy if the consequences are worse than the risks being minimized. Choices should be based on good science, as clearly articulated by Administrator Reilly.

Thus, the research programs of the agency should be focused on a research strategy which can amplify the production of information, uncovering potential problems that need further elucidation by government or other sectors of society, and providing the leverage necessary to insure its collection.

I would like to call your attention to the last chapter of the HEI book "Air Pollution, the Automobile, and Public Health" that was published by the National Academy Press. In there you will find very detailed recommendations on how to

approach tiered testing of unknown entities, as well as focused recommendations on specific fuels and whole emissions.

I differ with Dr. McClellan on the need for the evaluation of whole emissions, particularly in the context of studying acute and subchronic effects. A series of studies that I reviewed in the HEI book clearly indicate that running wheel performance is exquisitely sensitive to engine tuning, photochemistry and so forth. This provides a quick bioassay on the effects of fuel mixtures and its interaction with engine performance characteristics: during acceleration, for example. Chronic evaluations are another matter; but if undertaken, this type of information is an inexpensive add-on.

The section on the solvent syndrome assumes increasing poignancy for me with the passage of time. The size of the exposed populations and the nervous system toxicity displayed by individuals inhaling high levels chronically brings me to the conclusion that the TSCA criteria are met for further testing. I would argue that the time for first tier evaluations are past, and that the issue demands bringing to bear state-of-the-art technologies to address this need. I am at loss on how to "kick start" this societal process, having advocated intense evaluation of this sort for a number of years.

Bruce Bauman, American Petroleum Institute (Did not attend meeting; however, submitted written comments as follows:

My comments focus on UST-related issues, as that was my primary assigned section. However, since I have also been active in soil and groundwater related research, I will also provide some comments on those topics.

UST Issues: From a brief review of the previous (1989) draft of this document, it would appear that little of the research that has been published in the interim period has been addressed in this draft. This is evident in the Introduction (pg. 1-20) where the UST population is characterized. The statement that 20-25% of the tank systems are leaking or are expected to leak in the next 3-5 years is over 5 years old, and does not reflect the current state of the tank population. The EPA Office of USTs has more

current statistics that document the current status of UST releases, UST removals, and upgrades. I would suggest obtaining current information from OUST before finalizing this report.

I agree that general issues raised as research needs are the appropriate ones (e.g., material compatibility; effectiveness of leak detection methods). However, especially regarding the former, there is no reference to a variety of papers published in the last three years that focus on the material compatibility issues. I have attached title pages from these papers, and would think they should be referenced in the report. Further discussions with trade associations (e.g., the Steel Tank Institute; the Fiberglass Petroleum Tank and Piping) who manufacture tanks, piping and associated equipment for UST installations would probably uncover additional information of relevance to future research. For example, the Steel Tank Institute has published a study on "Corrosion Analysis of Methanol/Fuel Blends on Carbon Steel."

I believe it would be especially fruitful to concentrate more on the compatibility of the various gaskets, flanges, seals, etc. that may be found in UST piping runs, than on the general compatibility of tank materials themselves. It might be useful to conduct brief telephone interviews of various California oil companies that have been operating methanol or M-85 USTs for several years now, to determine if any issues have surfaced from these operational tanks.

Regarding UST leak detection, I am aware of little open literature published addressing alternative fuels. Guidance from EPA since the implementation of the federal UST regulations has stated that if USTs contain methanol, they must be secondarily contained. Leak detection would thus be greatly simplified.

Soil/Groundwater Issues: As above, the current draft does not include references to a number of recently published papers that advance our understanding of alternative fuels or their components in the subsurface. I have enclosed title pages from those reports and papers. (Attachment 13).

Colome:

Both the "Alternative Fuels Research Strategy" and the "Pollutants from Motor Vehicles Issue Plan Number 17" documents represent a proactive effort on the part of the Agency staff to address issues of widespread concern to the public and to the scientific community. The problems addressed, both real and perceived, are sharply focused in these two documents and a path is outlined for systematically developing the knowledge and insight needed in order to formulate informed public policy.

The Agency staff present a clear picture of the serious gaps in our current understanding and in our ability to establish comparative assessments of health and ecological risk among the policy options available for alternative motor vehicle fuels. But I also had a deep frustration as I read these documents. While the Agency frames a rational approach for taking a proactive stance on an emerging issue, the resources available for implementing the plan are so inadequate to the task that the framework is certain to fail.

Instead of being rewarded for proactive thinking, which is likely to produce substantial future savings, the Agency is left with a skeletal framework for addressing the questions of motor vehicle fuels. This pushes the useful answers so far into the future that, in effect, we are left with the same old and inefficient posture of responding hastily to issues as they arise.

The economic and environmental consequences of choices among alternative fuels and transportation options touch every corner of American society. Surely we can find the vision to invest today in making national decisions with long-term future consequence.

References:

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CHARGE FOR THE REVIEW OF THE ISSUE PLAN FOR POLLUTANTS FROM MOTOR VEHICLES

1. Are the research priorities expressed by ORD's program consistent with the priority information needs for mobile source programs? Is it clear that only a very few high priorities are being addressed because of total available resources. The key question then is whether the few priorities chosen are the most appropriate. There are several dimensions to this question: priorities among fuels, priorities among disciplines, and priorities within a discipline.

- o For a given project area:
  - o Is the approach likely to accomplish the stated goal?
  - o Is the approach likely to produce the anticipated results that are described?
  - o Is the "duration" for the research reasonable?

Miller:

Overall, the research priorities for ORD's program are consistent with the information needs from mobile sources programs. However, there does not appear to be a need for early $600,000 expenditure on developmental effects of methanol for five fiscal years, inclusive of FY '93. This statement is made given the recent research results on pharmacokinetics from CIIT and in acknowledgment of the methanol work on developmental effects in primates being funded by HEI. A reallocation of a portion of these funds in FY '94 to other high priority issues, such as MTBE, would be warranted. The human health effects projects are provided more in detail than the projects in the other sub-issue areas, and this enables a more definitive statement concerning the likeliness of the project to accomplish the stated goals and the reasonableness of the approach for producing the anticipated results. Given the lack of detail for some of the other project descriptions, it is difficult to comment on the question of appropriateness of the goals and results. However, this reviewer is of the opinion that the resources allocated to the human exposure assessment of mobile source emissions are inadequate to accomplish the magnitude of the task. Moreover,

it would appear that the duration of the necessary research is understated and that the probability of successful completion of the project may be somewhat overstated.

Colome:

1. Are the research priorities in the Plan consistent with the research needs? All of the research priorities in the Plan are at least consistent with the research needs. Given the difficult choices that had to be made to establish priorities between disciplines and fuels, the consensus building and compromise necessary for this plan show. Since the research plan only makes a first stab at a major issue, it is important to admit that the current Plan will not meet the information needs for the risk assessment paradigm presented in the Alternative Fuels Research Strategy. Accordingly, it is virtually a certainty that the stated goals will not be met within the time frame and research outline of the Issue Plan.

Utell:

1. It is incredibly clear that only a few high priority issues will be addressed given the available resources. The specific plans are still far too vague to really determine if the selected approach is likely to accomplish the stated goals. Until specific research proposals are available, one cannot provide a meaningful commentary on whether the program will produce the anticipated results in a reasonable time frame.

2. From an overview of the entire research plan and considering what you know of the research from other institutions, will the program produce cohesive results that can be used to significantly advance understanding of air quality impacts and health risk characterization?

Miller:

The program has the potential to produce cohesive results that will contribute significantly to our understanding of air quality impacts and health risk

characterization for mobile sources. However, this potential is greatly diminished by the magnitude of the resources available to address the myriad number of important questions. As such, it is the opinion of this reviewer that the net impact of the research plan will only be a modest one.

Colome:

2. Will the collective research program, including from other funding sources and conducted outside of EPA, produce a cohesive program? The outlined program is cohesive and it should advance the state of understanding. I doubt, however, that information can be generated in time to assist in making the policy decisions that will be required on alternative fuels.

Utell:

2. Within the Issue Plan, there is an impressive effort to describe collaborative efforts among various federal and private research institutions. The plan is a step in the right direction in an effort to utilize research sponsored by both the private and public sector in understanding the potential risks from alternative fuels. I applaud the effort but only time will tell if the program will meet with success.

In reviewing the document, I would urge the Agency to consider establishing an outside scientific advisory committee to work with the responsible administrator in setting priorities. This would be a small advisory group with the charge to review specific funding decisions related to the proposed research agenda. Obviously, funding will be grossly inadequate for addressing the research needs; the EPA would greatly benefit from outside expertise before funding new efforts or disassembling long-standing, highly-productive programs.

Dr. Colome:

V. Research Priorities, B. Prioritization, Pg. 12, lines 18-31: In this section it would be useful to introduce the concept of initial scoping of risks. It may not be necessary, for example, to know the human exposure patterns and health effects for all classes of fuels and emissions. A compound having a potential health effect and no significant exposure pathway or a low toxicity product should receive lower priority

for further investigation. This concept was implied in the document but could be made explicit in this section.

Sub-Issue 2: Human Exposures, Project Area 2.1 Human Exposure to Mobile Source Emissions, Purposes and Goal, Pg. 21, lines 13-15: It is stated here that determination of exposure to methanol is a major objective. I do not disagree with that objective but the Issue Plan does not provide a justification or rationale for making methanol a priority. The logic should be developed and presented in the Plan.

Sub-Issue 2: Human Exposures, Project Area 2.1 Human Exposure to Mobile Source Emissions, Scientific Approach, Pg. 22, lines 12-22: In this section I fear that the exposure modeling exercise may run ahead of our physical or empirical understanding. The exposure modeling should develop hand-in-hand with, and be guided by, our understanding of health and ecological responses to environmental agents. For example, if a health outcome of principal concern results from long-terms exposures, it will not be necessary to consider microenvironmental mass balance models based upon "advanced three-dimentional flow models." In this case, we would seek a parsimonious model that could describe some of the long-term variation in exposure.

Sub-Issue 2: Human Exposures, Project Area 2.1 Human Exposure to Mobile Source Emissions, Scientific Approach, Pg. 23, lines 1-3: The argument is made that past studies have used carbon monoxide as an emissions surrogate for conventional fuels and that this surrogate status may not be valid for methanol and benzene. Since this lack of validity is only speculated, I would suggest that the assumption be tested first before new large-scale personal exposure studies are initiated.

Colome:

On review of the Motor Vehicles Issue Plan it is painfully obvious that the resources available are not in proportion to the challenge of the task. The alternative fuels program-mandated by Congress will not receive sufficient scientific scrutiny to adequately evaluate the risks of these new fuels compared to conventional fuels. This circumstance is all the more unfortunate when we recognize that the environmental benefits have not even been clearly demonstrated for the alternative fuels program. A

truly credible research plan would require several times the anticipated budget. Given the stakes involved in potential health and environmental damage, or the costs of ineffective or unnecessary controls, the investment in a properly supported research program is indeed minor.

Schreck:

VI. Research Plan, Sub-Issue 1: Emissions Characterization and Air Quality, Project Area 1.1 Development of Analytic Methods for Emissions Testing: The emissions analytic methods issue is critical to many of the late parts of the program, necessitating that highly credible measurements be taken as early in the program as possible. Therefore it seems logical to put more money and resources into this effort to shorten the delivery time. Naturally this project and 1.2 will benefit from exchanges with the Auto-Oil Program and other extramural research efforts.

Project Area 1.2 Characterization of Emissions from Vehicles: Emission characterization from alternative rules will be necessary for later human exposure estimation and dosimetry for toxicity testing. Again, this project should be accelerated since the quality of later projects depends on it.

Project Area 1.3 Real-World In-Use Vehicle Emissions Testing: There is some confusion as to whether this is Real-World Emissions or part of Atmospheric Transformations (doesn't cross-check with budget at end of document). This reader feels that Real-World emissions takes precedent, for now, over Atmospheric Transformations.

Sub-Issue 2: Human Exposures: Sections 2.1, 2.2 and 2.3 are progressively less concrete in deliverables. For productivity sake, for now, put resources onto the first program Human Exposure measurement (2.1); followed by Comparative Health effects (2.2) and Comparative Risks (2.3) only as resources permit.

Sub-Issue 3: Health Effects, Project Area 3.1` Determine Exposure-Dose Pharmacokinetics for Methanol: Why not study the pharmacokinetics of methanol in human and prospective animal models using something like table isotope tracers to elucidate the kinetics of the process which damages specific tissues?

Project Area 3.2 Developmental Effects of Methanol: The question raised by this project is whether developmental effects should be the metric by which the health effects of alternative fuels are compared. This might be justifiable if birth defects were an observable problem in fuel handling or an anticipated problem with any of these fuels at the expected use concentrations.

Sub-Issue 4: Health Effects Institute: No specific research issues to consider.

Sub-Issue 5: Scientific Assessment: Scientific Assessment.

Winner:

The Issue Plan shows the result of funding shortage as critical areas in the analysis of the EPA Motor Vehicles Pollutants Program are either under-funded or completely missing from the proposed research activity. In particular, the program focuses on analysis of emissions and impacts of pollutants on human health. There is no doubt that these topics are crucial areas for research.

Conspicuously lacking from the Issue Plan is a component of research earmarked fro ecological elements. The absence of ecological research from the Issue Plan does not reflect lack of interest but rather lack of funds. Reasons for including ecological issues in the Issue Plan include:

1. The mandate of the EPA includes environmental protection, i.e., one of the clients of the Agency is the air, water, soils, and other ecosystem components;
2. Some ecosystem components are sensitive to ambient levels of fuel combustion products. Results of research from the Corvallis Lab show ambient levels of formaldehyde reduce plant growth. These preliminary data suggest more study of plant responses to motor vehicle emissions is needed;
3. Vegetation can show quick responses to mitigation efforts. Thus research with vegetation can show whether changes in fuel chemistry or air pollution levels resulting from mitigation bring desirable environmental changes.

The Issue Plan should not develop research for analysis of emissions, analysis of transport, and analysis of ecosystems. Rather, there should be one plan that will result in specific risk assessments that include several features, including ecological systems.

Miller:

II. Problem Statement, Pg. 1, line 24: In this document, the number of CO non attainment areas to use oxygenated compounds is listed as 39, yet on page E-2, line 28 of the Alternative Fuels Research Strategy, this number is listed as 41. Which is correct?

Question 1.2. What are the evaporative and combustion emissions of vehicles of varying technologies operated under different conditions with conventional, reformulated, and alternative fuels? Pg. 4, line 10: Suggest the inclusion of the word "some" before the word "confirmation" in order to convey the spirit stated earlier in the document of collaboration and close cooperation between research institutes being needed to effectively address the issues at hand.

Question 2.2. What are the comparative health effects of conventional fuels, reformulated gasolines, and alternative fuels? Pg. 6, lines 13-18: This rambling sentence is awkward and difficult to follow.

IV. Relationship to Other Planning Issues and Organizations, Pg. 9, line 14: Insert the word "the" before the word "Chemical".

V. Research Priorities, A. Candidate Sub-Issues, Pg. 10: The phrase "funded FY '93 and beyond" really does not provide an informative basis for assessing part of the overall charge concerning whether the duration for the research is reasonable.

V. Research Priorities, A. Candidate Sub-Issues, Pg. 10, line 28: Concerning the discussion of the Health Effects Institute, it would seem that a high priority for EPA to relate to HEI would be the need for research on mobile source secondary emissions from alternative fuels and fuel additives, as opposed to continued work by HEI on ozone and other products related to mobile source emissions.

7. Related Programs, Pg. 11, lines 13-25: This reviewer does not know how to interpret the discussion of related programs and then classification as "low priority for this issue" in terms of the research. It would seem more appropriate to identify the linkages without giving a priority since these other issue research plans are not part of issue #17.

B. Prioritization, Pg. 11, line 27: The first five sub-issues at indicated to be of equal priority and are to be funded. While this reviewer would not agree that all five of these issues are of equal priority, a relative ranking absent the overall resources targeted for the sub-issues is largely meaningless. The current plan reflects an

attitude of "doing more with less" and belies the fact that significant infusion of resources is likely needed in order to adequately address the research issues.

B. Prioritization, Pg. 12, line 28: If one acknowledges that the mobile source sub-issues, when compartmentalized into research areas, are of equal priority, no indication is given in the document that ORD has adequate resources to effectively address the top areas within each of these categories. If the resources allocated to a high priority area are insufficient to adequately do the research, it would be better to shift these resources and effectively deal with a fewer number of sub-issues.

Project Area 1.2 Characterization of Emissions from Vehicles, Scientific Approach, Pg. 17, line 2: Control system deterioration is, in the opinion of this reviewer, one of the most important factors to consider because emission projections based upon well operating vehicles will tend to underestimate the contribution of mobile sources to urban air pollution. The fact remains that most Americans do not keep their vehicles well maintained.

Project Area 1.3 Real-World In-Use Vehicle Emissions Testing, Pg. 18, line 14: The discussion in this section on "real world use" vehicle emissions testing for super emitters raises some questions to effectiveness of the research approach. To what extent do states have vehicle emission testing requirements and state inspection programs? Indeed, if the presence of "super emitters" is the factor greatest influencing the predictability of models, such as Mobile 3 and 4, a more effective strategy would appear to be enforcing emissions and increasing the frequency of testing of vehicles. Is the intent of the proposed research to provide EPA with the data base needed to make such an argument?

Project Area 1.4 Atmospheric Transformation of Vehicle Emissions, Scientific Approach, Pg. 20, lines 12-23: The section on Scientific Approach needs to be reworked. It is difficult to follow what is being done versus what is being proposed to be done given the apparent incorrect mixing of verb tenses in some of the sentences.

Project Area 1.4 Atmospheric Transformation of Vehicle Emissions, Duration, Pg. 20, line 25: The discussion of duration for the atmospheric transformation studies would

imply that a more appropriate phrasing would be to indicate that the studies will be phased out in FY '93 as opposed to being completed in FY '93.

Sub-Issue 2: Human Exposures, Project Area 2.1 Human Exposure to Mobile Source Emissions, Duration, Pg. 23, line 16: The duration of human exposure studies for mobile source emissions is stated to last as long as is needed to "get the job done." While this reviewer agrees that it is a long term research project, the criteria for the definition of when sufficient advancements have been made, needs to be established a priori so that a reasonable assessment of success can be made at a future time or an evaluation as to the extent of progress still needing to be achieved.

Sub-Issue 3: Health Effects, Project Area 3.1 Determine Exposure-Dose Pharmacokinetics for Methanol, Scientific Approach, Pg. 25, line 3: While direct information on methanol metabolism is not available for the mouse, there is indirect information from the study of such compounds as 4-methyl pyrazole.

Sub-Issue 3: Health Effects, Project Area 3.1 Determine Exposure-Dose Pharmacokinetics for Methanol, Duration, Pg. 25, line 14: The discussion of the duration of the PB-PK modeling efforts for methanol indicate that this is unprecedented research and must be conducted in a step wise fashion. The use of the word "unprecedented" for the research is not clear to this reviewer. Moreover, there is not a compelling reason to do all of the research in a step wise fashion. For example, pharmacokinetics of methanol in human volunteers does not need to await the availability of a fully defined model of methanol disposition in the mouse and primate.

Project Area 3.2 Developmental Effects of Methanol, Scientific Approach, Pg. 27, line

5: Insert the word "be" before the word "subjected".

Project Area 3.2 Developmental Effects of Methanol, Duration, Pg. 27, line 14: This reviewer again questions the use of the word "unprecedented" when describing the nature of the research and its conduct. It is this reviewer's opinion that a full development of a biologically based dose response model for developmental effects

of methanol across multiple rodent species with extrapolation to humans is longer than a six year research program. The embryonic dosimetry portion alone should not be underestimated as to its complexity. This is further complicated by the fact that the project will address various concentration x time relationships at critical time periods in the development of the fetus. Despite this, the research should receive high priority, not only because of methanol issues, but because of the model approach being able to be extended to other developmental toxicants.

Sub-Issue 5: Scientific Assessment, Project Area 5.1 Assessments and Program Management, Pg. 29, line 10: The scientific assessment sub-issue described as Project Areas 5.1 and 5.2, with 5.2 being related to cancer assessment. The title for Project Area 5.1, Assessments and Program Management, is encompassing also of cancer assessment even though 5.2 address as cancer. Some introductory sentences under Purpose and Goal might proceed the definition of Project Area 5.1 to help the reader follow the delineation between the two Project Areas.

Sub-Issue 3: Health Effects, Pg. 34, line 27: The discussion of the reported effects for single day exposures and their usefulness for short duration exposure assessment for man is overstated, given the several orders of magnitude difference in the exposure level of the rodent studies compared to what humans are exposed to in combination with results from studies at CIIT in primates.

VIII. Resources, Pg. 37, lines 7-15: The relative ranking of priority between two and three would appear to be reversed. A higher priority should be given to improving remote sensors so that whatever field studies are conducted can be more complete.

VIII. Resources, Pg. 37, line 27: Apportionment of a potential $500,000 decrease in funding is listed. However, without knowledge of all of the research projects available in the various areas, this reviewer would not be willing to indicate agreement or disagreement with the ranking of cuts. This would appear better left to program managers within EPA who have a greater working knowledge of the existing research. As a minor note, the priority three for cutting on pharmacokinetic models is

listed as $368,000, yet the table on page 38 lists the entire program on pharmacokinetics as $363,000--which number is correct?

Estimated Resources for Pollutants from Motor Vehicles ($ in 1,000s), Pg. 38: Given that the statement is made on page 36 that resources for the Mobile Sources research program are assumed to remain constant from FY '93-FY '97, why repeat the numbers in each fiscal year? Simply delete the resources that are duplicated in FY '94-FY '97 and add a footnote indicating straight-line funding is projected. Relative to the disposition of funds among the five sub-issue and project areas, the emissions characterization and air quality at first glance appear to be out of balance with the rest of the program, particularly in relationship to health effects research. However, the impact of the Health Effects Institute funding, if channeled to mobile source emissions health effects work, does provide adequate balance. The concern of this reviewer is that other issues covering ozone, for example, may also be attributing the HEI resources to their plan. Sated another way, the entire Health Effects Institute funding is listed here under Mobile Sources, even though only a portion of the research dollars are going to the kinds of mobile resource issues identified in the Alternative Fuels Strategy document and in Issue 17 on Mobile Sources. This could provide a false impression of the extent of the health effects work directly related to emissions from motor vehicles.

Dr. Goldstein:

1. My assignment was to review the introduction and overview, hence my comments are based on those sections. The motor vehicle issue plan appeared consistent with the alternative fuels strategy as regards priorities among fuels and disciplines. The discipline that I reviewed for the latter plan, ecosystem air exposures and effects, is not included in the former, hence the question of priorities within the discipline is not relevant. I accept the reasoning, lack of sufficient resources, given for the exclusion of this subject.

2. I feel that the program will significantly advance understanding, but that is a very general objective, more suitable for an academic institution than an environmental protection agency. A more meaningful question is will the program

lead to significantly improved risk management; that is, an improved balance between reduction of environmental risk and control cost. To answer that question, a quantitative risk management framework is needed.

Dr. Jeffries:

In answer to Question 2, I do not believe that the program as explained to us is capable of producing "cohesive results that can be used to significantly advance understanding of air quality impacts and health risk characterization." This is because there is no way for the current program to treat secondary pollutants in the risk assessment process. This is because the atmospheric transformations program has been cut. Existing photochemical reaction mechanisms were developed for conventional fuels and their application in urban air shed models are constrained by having to make reasonable accurate predictions of an observed episode. There are no observed episodes for large scale alternative fuels use. Therefore, we must rely entirely on the model having predictive capacity. Predicative capacity is inferred from scientifically based formulation and by direct demonstration via testing with high quality, unambiguous relevant data. Actions that establish a model's predictive capacity for atmosphere fate are the elements that are missing in the plan and their absence will prevent a significant advance "in understanding of air quality impacts."

Miller:

2.2.2.1.3 Benzene, Pg. 2-50, line 27: A 1984 publication should not be referred to as recent.

Mauderly:

2.2.2.1.3 Benzene, Pg. 2-51, line 12: "increased."

Mauderly:

Pg. 2-51, line 14: "Zymbal gland tumors."

Wood:

2.2.2.1.4 Conventional Gasoline, Pg. 2-52: Where is the discussion of the neurotoxicity of conventional fuel constituents?

Schreck:

Pg. 2-53, lines 16-27--2.2.2.1.4 Conventional Gasoline, Noncancer Health Effects of Gasoline Combustion Emissions: "...support the stated need for a thorough study of the health effects of unleaded gasoline exhaust emissions and their transformation products."

Mauderly:

Pg. 2-54, line 8: Was the purulence thought to be due to the exposure, or to concurrent infections? The latter would seem most likely.

Mauderly:

Pg. 2-55, line 17: "Forced flows, or tidal flows"?

Mauderly:

Pg. 2-55, line 19: The term "necroscopy" is used in reference to animals, instead of 'autopsy', which refers to humans."

Wood:

2.2.2.1.4 Conventional Gasoline, Pg. 2-56, lines 26-30, lines 26-30: Incomplete see Wood.

Mauderly:

Pg. 2-57, line 2-3: The study is not adequately described before, as suggested.

Wood:

2.2.2.1.4 Conventional Gasoline, Noncancer Health Effects of Uncombusted Gasoline Emissions, Pg. 2-57, lines 8-10 and Pg. 2-58, lines 4-17: this data is Hazard Identification in humans. At least one target organ system is clear from this data: the nervous system.

Mauderly:

Pg.. 2-58, line 26: It is not clear what is meant by reference to the "maximum tolerated concentrations." If a point needs to be made that concentrations could have been higher, some context should be given for what parameter would be considered indicative of a "maximal tolerated concentration." The concept of MTD is currently debated, and there are ranges of both opinions and definitions. There are not comments on whether or not the other studies referenced in the section were done at MTD.

Mauderly:

Pg. 2-58, line 29: Were the "dogs" Beagles?

Mauderly:

Pg. 2-59, line 1: The point seems to be made that the study is of significance because it was long-term. The opposite would seem to be true. Five years is only about one-third of the lifespan of the subjects. Would the same be said or a rat study with exposures of 8-10 months?

Miller:

2.2.2.1.4 Conventional Gasoline, Carcinogenicity of Gasoline Combustion Emissions, Pg. 2-59, line 7: For the discussion of particulate matter related to cancer induction by diesel exhaust, references should be added to reflect that the cancers occur at exposure levels associated with the phenomenon of "lung overload".

Mauderly:

Pg. 2-60, line 6: Have unit risk values been estimated for gasoline particles, or is this a reference to the unit risk estimates made for diesel soot? Are they proposed to be the same?

Schreck:

Pg. 2-60, line 16, Carcinogenicity of Uncombusted Gasoline Emissions: "'aerosol" of unleaded gasoline to "vapors" of unleaded gasoline.

Pg. 2-61, line 23, Same.

Mauderly:

Pg. 2-61, line 1: Upon what data is the "total" based? In other words, what is the denominator used in this context?

Mauderly:

Pg. 2-61, line 16: This statement appears nonsensical. Is the author proposing that there are tumors that are not likely to be caused by "progressions" of lesions?

Mauderly:

Pg. 2-61, lines 16-19: I have no particular problem with the statement, but it raises an issue that is both interesting and important. If we decide that particular animal tumors should be ignored in human risk assessment because of "nongenotoxic" agents, or a response peculiar to a particular animal species, then the same concept would have to be extended to other cases relevant to this chapter. A prime example is the carcinogenicity of diesel exhaust in rats. On the basis that the tumors do not appear to be caused by chemical genotoxicity, occur only in one

species (to date), and occur only in the company of substantial other pathology, then the carcinogenicity of diesel exhaust in rats would have to be discounted. That has not yet been done.

Schreck

Pg. 2-61 to 2-62: "The discussion here points to the difficulty of actually studying the health effects of gasoline vapors. As stated, the vapors over gasoline in a tank or escaping during refueling are not of the same molecular composition as the fuel itself. Therefore the study referred to was actually a study of vaporized unleaded gasoline rather than of unleaded gasoline vapor. To do the study in question would require considerable additional technology to fractionate the vapors and only deliver the appropriate lighter fraction for inhalation.

Mauderly:

Page 2-63, line 9: There are more recent summaries than the 1990 EPA draft document.

Mauderly:

Pg. 2-63, line 24: It is not clear what "but" means here. How are symptoms and function changes being contrasted?

Mauderly:

Pg. 2-63, line 29: The ITRI reference should be referenced by author, not be institution.

Wood:

2.2.2.1.5 Diesel, Noncancer Health Effects of Diesel Combustion Emissions, Pg. 2-64, line 7: I am unfamiliar with this paper by Laurie.

Mauderly:

Pg. 2-65, lines 6-7: It is the CxT that is important, not the exposure concentration.

Mauderly:

Pg. 2-65, line 8: It should be noted that the same investigators failed to reproduce the carcinogenicity in NMRI mice in a later study. The reference given reported carcinogenicity in NMRI mice from both whole and filtered exhaust, another curiosity.

Mauderly:

Pg. 2-65, lines 17-18: It is not clear why the discussion is limited to these 14 studies, when there are about 32 reported.

Mauderly:

Pg. 2-66, lines 16-17: Why isn't the Heinrich et al. work referenced here? They also showed that filtered exhaust did not cause tumors in rats (although it did in mice).

Miller:

2.2.2.1.5 Diesel, Pg. 2-66, line 20-21: The studies cited as unpublished are now published.

Mauderly:

Pg. 2-66, lines 22-23: I'm not certain that carbon black has been proven to be "biochemically inert," or oven exactly what that means. It is certainly not biologically inert. Moreover, the point is not just that carbon black caused tumors at the same concentrations used in some diesel studies, but that the same concentrations (exposure conditions) of diesel soot were shown to cause tumors in the same study.

Mauderly:

Pg. 2-67, lines 8-9: What is the evidence (reference) that particle-adsorbed organics do not accumulate in the lung to any appreciable extent? I'm not certain that this is true, although it is sometimes assumed.

Mauderly:

Pg. 2-67, lines 12-16: Why not reference the Pepelko manuscript in which this estimate is published? Also, this estimate was not used in the 1990 draft document, as stated. It was only published recently, and used a completely different approach than taken in 1990.

Miller:

2.2.2.1.5 Diesel, Carcinogenicity of Uncombusted Diesel Emissions, Pg. 2-67, lines 29-30: This reviewer would not agree a chronic bioassay should be undertaken for exposure to uncombusted diesel emissions simply based upon potency estimates of possible components. Rather, exposure assessment data should also be factored into the determination of the need for chronic studies. This reviewer would find it unlikely that exposures in the United States are sufficiently high as to warrant such a study, given the many other priorities expressed in this alternative fuels research strategy.

Suter:

2.2.2.2.2 Aquatic Ecosystem Effects, Pg. 2-72: Begins by describing some relatively well studied spills but then states that "above all adequate data on the response of actual ecosystems to exposure to fuels is lacking." The latter statement is used to justify a call for tests in "experimental ecosystems." Before that is done, you should determine whether observed effects in the field are predictable from laboratory toxicity studies. If not, you should determine why they fail and whether such systems would correct the likely cause of the failure.

Winner:

2.3 Research Needs: The rationale and background for the Alternative Fuels Research Program should be linked to other relevant EPA Research Programs. More information on benefits from expected O3 CO reductions from alternative fuels use should be included. In addition, information from the EPA Global Change Program. For example, data on CO2 and methane emissions trends and impacts would be especially useful.

Suter:

Pg. 2-87: I agree with the strategy of using case studies. The EPA should consider using real cases such as the 1988 Monongahela River spill.

Schreck:

2.3 Research Needs, 2.3.2 Effects Assessment, 2.3.2.1 Human Health Effects, Pg. 2-90, lines 8-18: PRIORITIES: ...the first (unleaded gasoline) is appropriately first, the second (constitute) really depends on the outcome of the first tests, and the third (diesel emissions) is of pretty low relevance for the US because of the lack of interest in diesels.

Miller:

2.3.2.1.2 Combusted Gasoline, Pg. 2-91, line 22: Insert the word "be" after the phrase "will need to".

Miller:

2.3.2.1.8 Research Objectives, Pg. 2-94, lines 10-13: Why spend valuable resources studying gasoline powered vehicles classified as "super emitters"? A better use of the dollars would be to implement testing and maintenance inspections for vehicles to comply with emissions. One will always be able to find a super emitter that will have a much greater yield, but this is letting the extreme situation dictate instead of the potential norm.

Winner:

2.3.2.2 Ecosystems Effects: Ecosystem components should be emphasized more so than in the current plan. Ecosystems responses to emissions from alternative fuel combustion are likely, as shown by preliminary studies an array of plants exposed to formaldehyde concentrations known to occur in southern California. In addition, ecosystem responses to pollutants produced from the use of alternative fuels will affect agricultural productivity, forest growth, aesthetic values, and ecosystem services provided to all residents in the air shed. Ecosystem components, including air, soil, water, and vegetation should be viewed as an integrated system rather than as independent elements. Ecosystem sinks for pollutants should be identified.

Mauderly:

Page 2-95, line 4: What is the human biomarker for diesel exhaust that should be validated? I'm not aware that any exist today that would allow us to "validate the use."

Suter:

2.3.2.2.2 Aquatic Ecosystem Effects, Pg. 2-97-99: Rather than jumping into microcosm and mesocosm studies, do the toxicity testing, then estimate effects for the exposure cases, and finally decide from the results of that exercise what more realistic testing or effects modelling is needed. In other words, rather than going through a prescribed series of tests like the old hazard assessment schemes, use the results of one set of tests to estimate risks, define an assessment strategy for the next assessment iteration that would resolve critical uncertainties, and then decide what further testing is needed for that assessment.

Pefley:

3.0 Methanol: The literature suggests that the greatest health risk has to do with mixtures of gasoline and methanol--M85 for example. These blends are being handled by vehicle service personnel as though they are gasoline. Yet, the literature suggests that absorption through the skin is increased with mixtures above either gasoline or methanol. If this is provable, early guidance in the handling of these blends by EPA would be valuable. This study needs to be included and given a high priority. This same issue may apply to E85 and other blends of ethanol and it should include blends of reformulated gasoline with methanol and ethanol.

In this Chapter on methanol a discussion of reformed methanol as a formaldehyde eliminator in cold weather startup would be in order. The highest risk problem arena for FFV's using M85 or M100 would be a high rise public garage on a still cold night after a public event. The carbon monoxide can be lethal and the formaldehyde could cause people to abandon their vehicles. The technology is potentially available for the generation of reformed methanol during the start and drive away of a cold vehicle under such circumstances and it could negate both the formaldehyde and CO issues.

To accomplish the above through support for such research not only eliminates the need for elaborate formaldehyde studies, but also has the potential of creating private sector jobs.

Miller:

3.1.2 Effects Assessment, 3.1.2.1 Human Health Effects, Pg. 3-14, line 3: This reviewer agrees that M100 should be relegated to minimal research activity, except for possible emission characterization studies. However, no health studies are warranted at this time.

Schreck:

3.0 Methanol, 3,1.2 Effects Assessment, 3.1.2.1 Human Health Effects, Pg. 3-14, lines 1-9: Since M100 will probably not be used in the quantities that M85 will, it is logical to put resources onto M85 studies rather than splitting funds to do M100 work also. Also, it seems prudent to hold on the DMS health effects work until atmospheric studies indicate that the exposure is occurring or will be significant as the fleet size builds.

Miller:

P. 3-15, Mixtures: Discussion on the proposed research for mixtures is sufficiently vague that adequate critique of the research is not possible.

Miller:

3.1.2.1.1 Individual Pollutants--Methanol and Formaldehyde, Pg. 3-15, line 1: Reference should be added to tell the reader about the metabolic relationship between formaldehyde and methanol.

Mauderly:

3.1.2.1.1 Individual Pollutants--Methanol and Formaldehyde, Pg. 3-15, line 5: This seems to be the only place in the document that recommends consideration of "interactive toxicity". The issue of interactions between any of the materials covered in this document and other agents could be raised, but it appears only here.

Miller:

3.1.2.1.2 Mixtures, Pg. 3-16, lines 9-13: The resolution implied from the studies to be able to sort out microenvironmental from ambient air effects is largely overstated. Unless extremely high spikes of micorenvironmental exposures are found from monitoring studies, this reviewer would suggest that concentration response studies be done for ambient exposures, since the high level exposures in these experiments could be extrapolated to spike type of exposures as a conservative estimate of potential exposure-response outcomes.

Schreck:

3.1.2.1.2 Mixtures, Pg. 3-16, line 20: Field studies following the introduction in a city would be very desirable in identifying the exposures in garage and other microenvironments and for refueling. This work should logically precede much of the clinical studies research.

Schreck:

3.2.2 Effects Assessment, 3.2.2.1 Human Health Effects, Pg. 3-49, lines 3-17: Same comments as Pg. 3-16, line 20 plus a reemphasis of the statement of the thought in line 16 that no published data exists on inhalation of M85 and that these fuel exposure studies will do a lot of defining the true chemical nature of the exposure during refueling or in parking garages. This will also form the basis for chronic inhalation studies of uncombusted M85, since like gasoline itself, M85 is a mixture of hydrocarbons with different boiling points so that it can not simply be vaporized to produce an exposure equivalent to a refueling or garage scenario.

Miller:

Pg. 3-50: The issue raised about methanol inhalation and its contributions to format levels is a non-issue given recent data presented by McClellan (CIIT Activities 13:1-7, 1993) and by Dorman et al. (Toxicologist, Abst. #629, p. 179, 1993) that demonstrate that methanol exposures to 900 ppm contribute insignificantly compared to endogenous format levels from normal metabolic pathways.

Mauderly:

3.2.2.1.1 Methanol, Pg. 3-50, line 26: It is not clear if the author is suggesting that "metabolism" represents a route of clearance that differs from renal. What other (non-renal) routes would metabolites take?

Schreck:

3.2.2.1.1 Methanol, Pg. 3-51, line 15: The fact that methanol levels in rats and monkeys were the same after an equivalent exposure period does not mean that the rat is a surrogate for the monkey or that either of them actually model the toxic phenomenon in humans. Since the toxicity is produced by the metabolites of methanol, the concentration and exposure time *in vivo* to these metabolites is an essential requirement for any animal model.

Miller:

3.2.2.1.1 Methanol, Pg. 3-51, line 19: Dorman et al. (Fundam. Appl. Toxicol. 20:341-347, 1992) have shown that female minipigs do not appear to be overtly sensitive to methanol and may not be a suitable animal model to study acute methanol-induced neuro-ocular toxicity.

Wood:

3.2.2.1.1 Methanol, Pg. 3-52, lines 1-13: This touches on my principal concern about methanol, that there may be damage to visual or motor function that is irreversible and independent of acidosis. If it is not independent of acidosis, the problem is of less concern. Neurotransmitter level changes after methanol exposure tell you nothing of importance, in all likelihood, unless they are irreversible. Ethanol would do the same without lasting sequealae, I presume.

Miller:

3.2.2.1.1 Methanol, Pg. 3-52, line 20: The extended primate studies by the Japanese for the 100 ppm exposure level for seven months should hardly be considered to be low exposure levels given the length per day of the exposures.

Schreck:

Pg. 3-52, line 26: Our experience with human exposures to methanol at these concentrations and above was that 75 minutes is too short a time period for methanol levels in the blood to rise to equilibrium values.

Schreck:

Pg. 3-53, line 10: Additional studies by Barabec et al further confirm the findings of Cooper et al, 1991.

Miller:

3.2.2.1.1 Methanol, Pg. 3-54, line 7: Bolon et al. (Fund. Appl. Toxicol, "Developmental toxicity induced in CD-1 mice by maternal methanol inhalation during embryogenesis," in press, 1993) have studies developmental effects at 5,000 to 15,000 ppm of methanol. Other work at 2,000 ppm is available (Rogers, in press) from EPA scientists.

Miller:

3.2.2.1.2 Formaldehyde, Pg. 3-55, line 21: The .03 ppm minimal sensory irritation level in humans appears inconsistent with the current threshold limit value of 0.3 ppm.

Wood:

3.2.2.1.2 Formaldehyde, Pg. 3-56, 57: This section would benefit by referring to Alarie's work where he demonstrated sensitization to formaldehyde that was context dependent, thus demonstrating the conditionability of some physiological responses to formaldehyde. If the other literature is not appropriately controlled, the levels at which sensitization occurs may be overestimates, or false positives.

Mauderly:

3.2.2.1.2 Formaldehyde, Pg. 3-56, line 20: What are the "high levels" to which dialysis nurses are exposed? These exposures need to be put into context.

Miller:

3.2.2.1.2 Formaldehyde, Pg. 3-58: The previous cancer risk estimates for formaldehyde are cited. Even though the EPA risk assessment document is currently under revision, some information should be given relative to the use of DPX and primate data in the revised risk estimates.

Mauderly:

3.2.2.1.2 Formaldehyde, Pg. 3-60, line 10: Considerable emphasis is placed on CIIT as the source of research on formaldehyde, and indeed, CIIT has done a lot of good work in this area. This emphasis is not necessarily wrong, but looks out of place because the institutions of all the other researchers in the document are not given. The authors should take care that this section does not appear as a commercial for CIIT (as it does now).

Miller:

Pg. 3-60, line 22: Strike the "s" on the word "accounts".

Miller:

3.2.2.1.2 Formaldehyde, Pg. 3-61, line 7: Insert the word "of" after the word "incidence".

Miller:

3.2.2.1.2 Formaldehyde, Pg. 3-61, lines 25-30: The work by Monticello et al. (Toxicol. Appl. Pharmacol. 111:409-421, 1991) on the regional increases in rate nasal epithelial cell proliferation following acute and subchronic inhalation of formaldehyde should be discussed. These investigators looked at changes in various sites in the nose after exposure to 0, 0.7, 2, 6, 10 or 15 ppm formaldehyde for up to 6 weeks. While a direct correlation between sites susceptible to formaldehyde induce nasal cancer and increased cell proliferation was not found, a clear correlation between sites of cellular injury and increases in cell proliferation were shown, as well as a

concentration dependent response which correlated with the previous published results from the bioassay.

Miller:

3.2.2.1.2 Formaldehyde, Pg. 63, line 18: The Casanova et al. in press reference is now citable. In addition, analyses by Casanova and Heck on the subject of DPX in various species has been addressed in CIIT Activities 1991; 11:1-6.

Mauderly:

3.2.2.1.2 Formaldehyde, Pg. 3-64, lines 17-20: The intent of this statement is not clear. The author should clarify the linkage between the location of cross-links and the locations of human tumors.

Miller:

3.2.2.1.2 Formaldehyde, Pg. 64, line 21: The long term studies referred to in this sentence relative to DPX exposure have been addressed by Heck and Casanova. See the abstracts for the 1993 Annual Meeting of the Society of Toxicology.

Mauderly:

3.2.2.1.2 Formaldehyde, Pg. 3-64, lines 23-26: Again, the intent is not clear. The author should clarify the linkage between the location of cross-links and the locations of human tumors.

Mauderly:

3.2.2.1.3 Dimethyl Sulfate, Pg. 3-65, lines 1-20: First, what kind of hamsters, rats, and mice? Second, what was the exposure pattern? The concentration alone isn't sufficient information.

Schreck:

3.3.1.4 Analytical Methodology, Research Objectives, Pg. 3-94, line 12: "Definitely agree that these measurements are needed first (highest priority) for planning of follow-on studies."