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FROM Melanie Marty, Ph.D.

SUBJECT Comments on risk assessment bulletin

COMMENTS _____

California Environmental Protection Agency

The energy challenge facing California is real. Every Californian needs to take immediate action to reduce energy consumption.

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Office of Environmental Health Hazard Assessment



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Arnold Schwarzenegger
Governor

June 15, 2006

Office of Information and Regulatory Affairs
Office of Management and Budget
725 17th St., N.W.
Washington, D.C. 20503

RE: OMB Risk Assessment Bulletin

To Whom It May Concern:

The California Environmental Protection Agency, Office of Environmental Health Hazard Assessment (OEHHA) is appreciative of the opportunity to comment on the Office of Management and Budget's Risk Assessment Bulletin. OEHHA is the primary risk assessment entity within Cal/EPA and is responsible for health risk assessments of toxic air contaminants, drinking water contaminants, and other environmental contaminants. We have many years of experience with risk assessment under a variety of programs and we hope that you find these comments useful.

If you have any questions, please call me at (510) 622-3154.

Sincerely,

Melanie A. Marty, Ph.D., Chief
Air Toxicology and Epidemiology Branch

Enclosure

California Environmental Protection Agency

The energy challenge facing California is real. Every Californian needs to take immediate action to reduce energy consumption.

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Introduction

The Office of Environmental Health Hazard Assessment is the main risk assessment entity within the California Environmental Protection Agency. We have many experienced risk assessors and scientists from a variety of disciplines on our staff and we conduct risk assessments for toxic air contaminants, drinking water contaminants, and soil-borne contaminants. Our scientists prepare health effects assessments on a variety of chemical contaminants including carcinogens, reproductive toxicants, and developmental toxicants. We also provide risk assessment guidelines to our sister agencies and develop health-based recommendations for California's Ambient Air Quality Standards.

General Comments

Although the purpose of the Office of Management and Budget's Risk Assessment Bulletin, as stated on page 3, is "to enhance the technical quality and objectivity of risk assessments prepared by federal agencies by establishing uniform, minimum standards" it is not clear why there is a need for this Bulletin. Nothing in the preamble indicates widespread problems with existing risk assessment guidelines from U.S. EPA or any other agency. The U.S. EPA has gone to great lengths to evaluate risk assessment models, to standardize risk assessment protocols, and to apply new information and models when they are scientifically justified. In contrast to its stated purpose, the Bulletin seems to contradict some of the practices delineated in existing well-reviewed risk assessment guidelines produced by U.S. EPA.

In general, the Bulletin does not provide additional information to improve the technical quality of risk assessments. The Bulletin seems to call for additional analyses to be included in almost all risk assessments and ignores the broad expertise of federal agencies including the various technical risk assessment guidelines that U.S. EPA has written and which have been fully vetted in public and peer reviews.

One of the most significant problems with the Bulletin is the broad definition of risk assessments ("publicly available" and "influential" risk assessments) to which all or part of this Bulletin would apply. While some of the standards are generally in practice, many are not necessary or are not achievable given limitations in available data, models, resources, etc. Application of the "standards" would result in:

- "paralysis by analysis" for many risk assessments;
- loss of transparency as the extensive analysis required by the standards would make the risk assessments more opaque; and
- no improvement in the risk assessments because of unwarranted analyses of alternative models, model uncertainty, etc. in the absence of appropriate data.

Extensive analyses should be reserved for very important risk assessments and should be conducted only if there are data to support the additional analyses.

Another significant problem is the overemphasis on "central estimate" of risk, found in several places in the Bulletin. The central estimate is not more accurate, as the Bulletin

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seems to imply, than a higher percentile on the distribution. Central estimates are subject to variability and uncertainty in underlying data and are not the "true" estimate of risk. There are valid reasons for risk assessments to focus on higher ends of the distribution of exposure and risk – use of values on the higher end of an exposure or risk distribution is done to account for underlying variability in the population in both exposure and susceptibility.

Finally, although fairly short, the Bulletin is very difficult to read and understand. It seems to be written by individuals not involved in actually conducting risk assessments and would benefit from editorial review and revision.

Specific comments by section and page number:The Requirements of This Bulletin. Section I. Definitions, and Section II. Applicability

Page 8 – The bulletin's definition of risk assessment is very vague. The USEPA has their own definition of chemical risk assessment which is more useful than that presented here, and includes the standard steps of hazard assessment, exposure assessment, dose-response assessment, and risk characterization. The bulletin does not explain why there is a need to overwrite EPA's definition of risk assessment.

Page 9 – Most of the standards in the bulletin are meant to apply to any publicly available risk assessment (in other words, all risk assessments) and additional standards are meant to apply to "influential risk assessments". "Influential risk assessments" is quite broadly defined, certainly more broadly defined than EPA's Peer Review Guidelines or their Information Quality Guidelines. The examples of influential risk assessments in the bulletin include reference doses and reference concentrations, margin of exposure analyses, IRIS values, and so on. There is no real differentiation in this bulletin and in the definition of influential risk assessment between a risk assessment that really has large influence and one that does not. Since the bulletin calls for additional analyses of alternative risk models, alternative data sets, and so on, for every influential risk assessment, the potential is great for a serious slowing of risk assessment without a parallel increase in knowledge. While the last paragraph on page 9 states that the "rule of reason" should prevail in applying the requirements of the bulletin, the requirements to apply extensive analyses to conform to the requirements in the bulletin for anything other than a screening level assessment, is in direct contrast to the rule of reason. EPA provides much-needed information to state agencies charged with environmental and public health protection. Requiring EPA to do many more analyses to determine model uncertainty, ranges of plausible estimates, and so forth, will slow EPA's risk assessment information flow to the states and negatively impact control and clean-up at the ground level without providing, in most cases, any more information on risk.

An Agency should have the option of determining which analyses require extensive uncertainty assessment and which do not. U.S.EPA with its 30 years of experience

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conducting risk assessment and the open process used to develop its public and peer-reviewed guidelines is capable of determining what risk assessments should be considered influential and what should not. While the Bulletin allows the Agency Director limited prerogative to waive the standards, the Agency Director is not routinely involved in risk assessments at the beginning of the process (e.g. for typical IRIS assessments).

Section III. Goals

Page 10. The preamble to the bulletin describes "Goals" for each risk assessment. The first goal (Goals Related to Problem Formulation) describes the need for iterative dialogue with the agency decision maker who will use the assessment. A caution is warranted here such that risk management does not overly influence the risk assessment. This important separation of risk assessment and risk management is not even mentioned in the Bulletin and should be discussed.

Page 10-11. Goals Related to Completeness. The text describes the tension between the desire for completeness and for practical and relevant information needed to address the risk. The section mentions the OMB Information Quality Guidelines and Peer Review Bulletin. These documents have a narrower definition of influential risk assessment that is more appropriate than the one in this Bulletin. The application of these standards to influential risk assessments as currently defined will result in unrealistic expectations for detailed and costly analyses for almost every risk assessment beyond a screening level. Thus, there is internal inconsistency between the preamble and the actual Bulletin, as well as between the Goals in the bulletin (Section III) and many of the requirements in Sections IV and V.

Section IV: General Risk Assessment and Reporting Standards

Page 13. Standards Relating to Scope. On the second page, the first full paragraph mixes up several concepts. The last two sentences seem to imply that effect modification (termed risk-modifying in the bulletin), synergism and confounding are all the same. This section should be reworded, preferably by someone who is familiar with the conventional uses of those terms.

Page 13. Standards Related to Risk Characterization. The second sentence states that "When a quantitative characterization of risk is provided, a range of plausible risk estimates should be provided." This might be much easier to do in some instances than in others. This requirement for all risk assessments available to the public, including all IRIS assessments (RfCs, RfD,s, cancer potency factors), is very unrealistic. For instance, what does it mean to provide a range of plausible risk estimates when developing a Reference Dose? Generally, for noncancer health effects, EPA chooses a standard protective of sensitive subpopulations or lifestyles – how does one provide an estimate of

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plausible ranges of risk in this case? This standard needs to be revised to indicate when it might be appropriate to do so.

Page 15. Standards Related to Critical Assumptions. This section states that "Whenever possible, a quantitative evaluation of reasonable alternative assumptions should be provided." This may seem, at first glance, like a reasonable requirement, but such an analysis could be very resource-intensive, and may not be a reasonable approach for every assessment. The EPA has risk assessment guidelines that have undergone extensive public comment and peer review. As part of these guidelines, specific model inputs, most of which are data-derived, are chosen as defaults by the Agency; thus, these guidelines provide the risk assessor with peer-reviewed assumptions based on available data to use to fill data gaps. Taken to the extreme, this standard could be interpreted to mean that any other defaults and alternative assumptions and resulting risk estimates need to be described in all publicly available risk assessments. The purpose of risk assessment guidelines is to standardize the approaches; this has been done in the various U.S.EPA risk assessment guidelines after much public and scientific peer review. This standard, and others, undermines that process.

Page 16, number 3, under "Standards Related to Regulatory Analysis". The standard states "The risk assessment should include information on the timing of exposure and the onset of the adverse effect(s) as well as the timing of control measures and the reduction or cessation of adverse effects." This is not a meaningful statement and appears out-of-context. The outcome of a control measure or regulatory action is a reduction in risk of adverse health effects. The timing of exposure and onset of adverse effect may be known from animal studies, or possibly human studies, but has little relevance to implementing a control measure. If one interprets this statement to mean that the risk assessor should guess when cancers might be reduced by reduction of exposure to carcinogens, then it is an impossible requirement.

Page 16, same section, number 5. The "standard" indicates a range of plausible risk estimates should be reported with a central estimate. The bulletin states that the central estimate can be a mean or average of the distribution or "a number which contains multiple estimates of risk based on different assumptions, weighted by their relative plausibility". It is generally not appropriate scientific practice to combine estimates made from different models to come up with an average.

This "standard" brings up another issue. Since U.S.EPA tries to protect the majority of the population, and sensitive members of the population are not "average", where does use of the central estimate of risk come into play? Is the standard implying that regulatory action be based on the average person? Do asthmatics, children, ill and elderly people fall out of the equation at this point? Would the risk assessor need to have central estimates for each sensitive subpopulation considered in the assessment? This standard should be revised to address these concerns.

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Special Standards for Influential Risk Assessments

Page 16. As noted above, the definition of influential risk assessments is vague and appears overly broad and in conflict with the OMB Information Quality Guidelines and Peer Review bulletins, and with U.S.EPA's implementation of these guidelines. Thus, as it stands, the "standards" in this section would seem to apply to everything beyond a screening risk assessment.

Page 17, Standard for Comparison to Other Results. This standard states "...it is appropriate for an agency to find and examine previously conducted risk assessments on the same topic, and compare these risk assessments to the agency risk assessment. A discussion of this comparison should be incorporated into the risk assessment." This requirement needs some boundaries. The requirement will be a substantial waste of resources for the EPA. EPA has worked hard at developing risk assessment guidelines which have been peer-reviewed and reviewed by many stakeholders. Anyone with a vested interest can conduct a risk assessment with irrelevant or unscientific and biased inputs to get the desired result. Why would the Agency have to respond to these assessments which have no basis in environmental health sciences, have not been peer reviewed, and were not conducted in accordance with public- and peer-reviewed risk assessment guidelines? This standard should be removed or modified by indicating the Agency should compare to previous U.S.EPA assessments or those conducted by other relevant public health or environmental agencies.

Page 17, Standard for Presentation of Numerical Estimates. The standard implies that presentation of a single estimate of risk is always misleading and always provides a false sense of precision. This statement is unfounded. EPA and state agency risk assessments typically describe uncertainties either qualitatively or quantitatively, and describe the reasons for choosing the key studies, which underlie a chemical specific risk assessment, as well as key assumptions. Presenting a range of risks, in our collective experience, does not help convey "a more objective characterization of the magnitude of risks". In some cases, the data are simply not available to present a credible range of risk estimates. As noted earlier, this Bulletin appears to have been written by people with little to no on-the-ground risk assessment (or risk communication) experience.

Also under this standard, it is stated that "This bulletin uses the terms "central" and "expected" estimate synonymously". It describes using a weighted average from different models to come up with the "expected" or "central" estimate. Such a practice is not generally appropriate as one is "averaging" apples and oranges. The section ends by stating, "Formal probability assessments supplied by qualified experts can help assessors obtain central or expected estimates of risk in the face of model uncertainty". This type of expert elicitation is neither standard nor has it undergone the extensive public and peer review conducted for the existing USEPA risk assessment guidelines. When there is an underlying lack of knowledge resulting in insufficient information to develop a distribution for a toxicity-based risk estimate, then the results of expert elicitation are themselves speculative. In other words, there is no improvement in the uncertainty by

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asking various experts their opinion. Furthermore, the outcome of such an expert elicitation depends highly upon the composition of the experts, and whether they have any knowledge of epidemiology, toxicology, public health, or risk assessment. Finally, the cost associated with expert elicitation is very large and it is totally impractical to do this for every "influential" (as defined in this bulletin) risk assessment.

Page 17-18, Standard for Characterizing Uncertainty. The bulletin would require influential risk assessments, broadly defined, to include an uncertainty analysis. As noted already, not all risk assessments warrant conducting an uncertainty analysis. Because the Bulletin so broadly defines influential risk assessment, this standard should be removed, or additional clarification regarding when uncertainty analysis is appropriate should be added. On page 18, the bulletin defines the difference between the results of models as "model uncertainty". This is inaccurate. Some models may be much more uncertain than others – the uncertainty is a property of the model not the numerical differences between the results of two models. The standard also requires the risk assessor for an influential risk assessment to perform multiple assessments with different models and report the extent of the differences. Again, this is a resource intensive undertaking that may be totally uninformative, particularly where one model is much more likely to be the best model than another. Why use a nonlinear model with a mutagenic carcinogen, for example, when the USEPA public- and peer-reviewed risk assessment guidelines (and much data underlying these guidelines) clearly indicate that linear models are appropriate for mutagenic carcinogens?

The standard notes that the risk assessor should "document and disclose the nature and degree of statistical uncertainty on input parameters". While this might be useful in some instances, in general, this requirement would take tremendous resources if it were applied to every input parameter. EPA has developed a wide range of exposure parameters for use in risk assessment at considerable cost to help standardize inputs as well as develop the best possible parameters given available data. There would be no point in going back to describe statistical uncertainty in all these parameters. This requirement should be deleted, or at a minimum the standard should require the assessor to describe statistical variability in only very key model inputs, where feasible.

Page 19. Standard for Characterizing Results. This standard would require influential risk assessments to present results based on different adverse health effects observed in studies, and on different studies in the database. When conducting a chemical-specific risk assessment, the initial steps involve exhaustive review of the literature and available studies, and decisions on which studies are most appropriate for the quantitative risk assessment (based on study quality and a host of other factors). The risk estimates are made for the most sensitive adverse health effect, which would provide protection against all the observed adverse health effects. While it makes sense to estimate Reference Doses, for example, using the best studies available and compare the estimates from key studies in the database, it would generally be uninformative to provide risk estimates for every possible adverse health outcome and study.

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Page 20. Standard for Characterizing Human Health Effects. This section indicates that the determination of adverse health effects "shall be specifically identified and justified based on the best available scientific information generally accepted in the relevant clinical and toxicological communities". To our knowledge, there have not been any U.S.EPA risk assessments which did not identify the adverse health effect that was the basis for the assessment. In addition, most clinicians have no expertise in risk assessment. Further, the underlying implication is that an adverse health effect must be clinically relevant. This is not consistent with standard accepted risk assessment practices. A shift in population distribution of risk factors due to environmental exposure (e.g., a reduction in IQ from lead exposure) is certainly an adverse health outcome, but not necessarily something that is clinically relevant for a specific individual.

There is an additional requirement in this standard that when qualified experts disagree, the extent of differences should be disclosed in the risk assessment. If that is the case, then the qualified experts need to disclose who is paying them and whom they represent.

Page 20. Standard for Discussing Scientific Limitations. This standard indicates that a risk assessment should include discussion regarding the nature, difficulty, feasibility, cost and time associated with undertaking research to resolve a report's key scientific limitations and uncertainties. It is not at all clear what this requirement adds to a risk assessment, particularly with such a broad definition of "influential risk assessment". In many if not most instances, the risk assessor would have to speculate about the cost and time associated with undertaking research to resolve uncertainties.

Page 21. Standard for Addressing Significant Comments. The standard indicates that "scientific comments shall be presumed to be significant", and that where the Agency takes a different position than a commenter, the Agency should provide an explicit rationale for why the agency has not adopted the position suggested by the commenter. While addressing public comments is generally quite useful and adds rigor to risk assessments, it is likely not necessary for every risk assessment to address all cases where the Agency takes a different position than a commenter. Cal/EPA receives sometimes voluminous comments on an issue – not every "scientific comment" is substantive or significant. That should be left up to the reviewing Agency to decide. That sentence should be struck from this standard.

Other Minor comments:

1. Page 6, under Types of Risk Assessments, Dose-Response Analysis – The third sentence of the first paragraph states "When sufficient numbers of people have been exposed to large doses of chemicals and radiation, it may be feasible to estimate risks using health data and statistical methods." The implication of this statement is that low dose effects cannot be measured in humans. The descriptor "large" in front of doses is a relative term, and should be replaced by sufficient, or some other descriptor. The field of environmental epidemiology, for example air pollution epidemiology, has progressed rapidly and scientists are measuring the health impacts of "low doses" of air pollution.

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Third paragraph – In the phrase “pathology can be performed on rodents to make precise counts of tumors or other adverse events”, the term “adverse events” should be replaced with “toxicological endpoints”. In addition, other experimental animals have been used besides rodents. This should be acknowledged in this section.