Comments on Proposed Revisions

to the Proposition 65

Prioritization Procedure

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OEHHA should retain the current Prioritization Procedure. The current procedure was adopted in 1997 after three years of analysis, more than five opportunities for public input and two well-attended workshops. The September 2004 proposed revisions to the Prioritization Procedure should not be adopted because they are (i) less scientific, (ii) too general, (iii) less open and transparent, (iv) less consistent with the statute's "clearly shown" standard, (v) more costly in staff and committee resources, and (vi) unnecessary.[1] Finally, the Proposed Revisions contradict prior expert panel input.

I. The Proposed Revisions Are Less Scientific

a. Prioritization should be open to new information

The Proposed Revisions make no allowance for changing a prioritization evaluation based upon new information. Considering and responding to new information is fundamental to the integrity of the prioritization process, obviously desirable from a scientific perspective, and a common-sense element of good government. Consideration of new information should not be removed from the Prioritization Procedure.

b. Prioritization should preliminarily examine complicated issues

Removing the evaluation of indisputably relevant "complicated scientific issues" from the prioritization process is clearly less scientific, and is one of the most significant changes in the Proposed Revisions. The Proposed Revisions state:

> "Complicated scientific issues concerning chemicals under consideration are not addressed in the prioritization process but may be addressed, as needed, in the development of hazard identification materials. For example, the relevance of a particular tumor type to humans, interspecies differences in toxicity or

[1] The existing Prioritization Procedure adopted in May 1997 is referred to herein as the "Prioritization Procedure" or the "Existing Procedure," and the draft revisions dated September 2004 are referred to as the "Proposed Revisions."

pharmacokinetics, or establishment of the most appropriate exposure metric in an epidemiology study will be examined in detail in hazard identification materials prepared for the CIC or DART IC consideration, rather than during the prioritization process." (OEHHA, 2004a).

This less scientific approach will have at least four significant adverse impacts.[2] First, the failure to evaluate important considerations of interspecies differences in tumor type or pharmacokinetics, for example, will cause the committees to operate less productively since fewer chemicals that do not meet the statute's clearly shown standard will be filtered out during the prioritization process. Under the Proposed Revisions, more chemicals will be added to the priority list and be reviewed by the Identification Committees that will, eventually, after the expenditure of unnecessary time and energy by staff and the committee, be screened out upon review of the relevant scientific data.

Second, the scientific dialogue between OEHHA and interested parties with respect to chemicals under review will be cut short under the Proposed Revisions. One of the key elements of the current procedure is "to get all the relevant data and scientific studies to the table early on so that when the information reaches the Science Advisory Board, the Science Advisory Board members have a complete and objective picture of the potential hazards posed by a chemical." (OEHHA, 1996). Since "complicated issues" would not be relevant to prioritization under the Proposed Revisions, interested parties will not be called upon to submit data on those issues as early in the process and OEHHA will not be called upon to advise the public of its preliminary analysis on those issues. In

[2] The procedure outlined by the Proposed Revisions appears to result in the submission of every chemical for which a Hazard Identification Document is prepared to the relevant Identification Committee for listing evaluation. Thus, review of the so-called "complicated issues" at the Hazard Identification stage will not permit any screening when the information reviewed warrants lowering the priority.

the past, having OEHHA's preliminary analysis of complicated issues has been of tremendous value to interested parties, and has guided the submission of supplemental data to OEHHA. The contrast between the current Prioritization Procedure's "triage" approach of allocating more time and effort to the prioritization of more complicated chemical evaluations and the complete failure to examine complicated issues in the Proposed Revisions is stark. OEHHA has not justified this less scientific approach and it should not be adopted.

Third, the Proposed Revisions only allow interested parties sixty days to respond to OEHHA's analysis of all the significant, complicated issues related to a chemical. This is not enough time and is not consistent with comment opportunities allowed by other entities engaged in hazard identification. For example, the NTP's CERHR uses two sixty-day comment periods to solicit comments on its Expert Panel Reports before the NTP issues its final monograph. Similarly, NTP's Report on Carcinogens normally allows interested parties at least six months to review the agency's analysis of a chemical and to provide input.

Fourth, the change from the Existing Procedure's statement that the appraisal "*will be made* on the basis of a scientific evaluation of the available information" to the proposal that the assessment "*could* be based on original research articles, or literature compilations or reviews" (emphasis added in both) clearly is less scientific and less consistent with the statute's emphasis on scientifically valid testing. This proposed change also begs the question of what else OEHHA believes an evaluation could be based on beyond "scientifically valid testing according to generally accepted principles," as described in the statute. (Cal. Health & Safety Code § 25249. 8(b)).

c. The proposed revisions wrongly limit maternal toxicity considerations

The Proposed Revisions wrongly limit the relevance of maternal toxicity and systemic toxicity to circumstances where those conditions "preclude interpretation of the study." In contrast, toxicologists generally agree that maternal toxicity and systemic toxicity observed at levels that are significant, but which do not preclude interpretation of the study, should be weighed in an overall assessment of the level of toxicological concern. Indeed, the USEPA document cited by OEHHA, which is a risk assessment document rather than a hazard identification document, makes clear that "it is important that the relationship of maternal and developmental toxicity be evaluated and described" in the final risk assessment. (USEPA, 1991). To the extent that this USEPA risk assessment document is relevant to the prioritization process for hazard identification, it counsels that an overall evaluation of maternal and developmental toxicity should be undertaken and described, not confined to an unduly narrow set of circumstances. The USEPA continues: "Although the evaluation of developmental toxicity is the primary objective of standard studies within this area, maternal effects seen within the context of developmental toxicity studies should be evaluated as part of the overall toxicity profile for a given chemical." (USEPA, 1991).

Casarett & Doull's Toxicology also recognizes that all maternal toxicity concomitant with developmental toxicity should be examined: "It is indisputable that material toxicity that is observed to be concomitant with developmental toxicity in testing protocols complicates the interpretation of the results for risk assessment." (Casarett & Doull, 1996).

II. The Proposed Revisions Lack Adequate Detail

The existing Prioritization Procedure contains 45 lines of appropriate scientific guidance concerning the determinations that govern whether a chemical will be assigned a "high" priority for Committee review.[3] In contrast, the Proposed Revisions to the procedure released in September 2004 as an "Update" merely contain 14 lines concerning prioritization determinations. Indeed, the Proposed Revisions merely note that "overall evidence" and "relevant information" will be considered "as appropriate." A side-by-side comparison is instructive:

Existing Procedure (May 1997)	**Proposed Revisions (Sept. 2004)**
"Evidence for prioritization will come from epidemiological or animal toxicity studies or other relevant data indicating the potential carcinogenicity or developmental/reproductive toxicity of the chemical."	"[T]he overall evidence of carcinogenicity or reproductive toxicity of the chemical would be considered, including epidemiologic, animal bioassay, and other relevant information, as appropriate."
"*Epidemiological studies*: The evidence considered will include the study population, exposure situation, tumor type or developmental / reproductive toxicity endpoint, nature of the dose-response curve, possible roles of bias and confounding, and quality of studies. In judging the epidemiological evidence, greater weight will be given to analytical epidemiological studies and lower weight to descriptive studies and case reports. Both positive and negative studies will be considered in assessing the overall level of hazard concern."	No discussion
"*Animal studies*: The evidence considered will include the number of experiments and species tested, route of administration, frequency and duration of exposure, numbers of test animals, and consideration of dose-	No discussion

[3] Sections 4.3.1 and 4.3.2 describe the "Basis for Assignment of Priorities" and "Level of Hazard Concern," respectively. These sections contain 45 lines of text. See Existing Procedure at pp. 8-9.

response. Both positive and negative studies will be considered in assessing the overall level of hazard concern."	
"*Other relevant data*: Evaluation of other relevant data for use in prioritizing candidates will also be made. Such data include information on mechanism of action, chemical structure, maternal toxicity, metabolism, and genotoxic activity."	"In accordance with guidelines of the U.S. Environmental Protection Agency (1991, 1996), adverse developmental effects that co-occur with maternal toxicity, and reproductive effects that co-occur with systemic toxicity would be considered evidence of reproductive toxicity unless these toxicities are so severe as to preclude interpretation of the study. In animal data evaluations, effects would be assumed to be relevant to humans, unless OEHHA determines there is sufficient evidence to the contrary."
"A qualitative appraisal of the potential for a chemical to cause cancer or developmental/reproductive toxicity will be made on the basis of a scientific evaluation of the available information."	"This preliminary overall evaluation could be based on original research articles, or literature compilations or reviews."

III. The Proposed Revisions are Less Open and Less Transparent

The Proposed Revisions are much shorter, much less specific, provide for less public input, and contain fewer objective criteria. Moreover, the Proposed Revisions expressly state that they will not even necessarily be followed by OEHHA. This completely discretionary approach to prioritization represents a fundamental reversal of OEHHA's ten-year emphasis on openness, objectivity and transparency from 1994 through 2004. OEHHA's management aptly summarized its prior decade of support for openness and predictability in a 1994 statement to the Carcinogen Identification Committee on prioritization goals:

> "[W]e're trying to set up a process that everybody can understand, and there are many perspectives that are brought to bear when looking at Prop 65. [¶] In the past, sometimes it's been hard to figure out how and where chemicals got

nominated, why some were advanced to being considered and why others didn't, and we're trying to change that equation by making it crystal clear what are the objective criteria by which chemicals are identified, how they are prioritized one against the other and, you know, when and where you [the Identification Committee] are going to start looking at these things."

(CIC, 1994).

OEHHA does not even pledge to adhere to the Proposed Revisions if they are adopted, instead providing an unrestricted statement that the Director may "modify" the new procedure "when necessary." In contrast, the Existing Procedure only may be modified in limited circumstances upon a finding that doing so would advance public health.

OEHHA began drafting the Existing Procedure in early 1994 after recognizing that its process was not sufficiently open, predictable and objective. More than three years later, after substantial public input and deliberation (four draft documents for comment and five opportunities for oral comment, including two dedicated workshops), OEHHA adopted the Existing Procedure in May 1997. The Proposed Revisions contain less than half the content of the Existing Procedure (11 double-spaced pages compared with 14 single-spaced pages) and virtually no details concerning how OEHHA will act. The Existing Procedure provides for a workshop on particularly complicated issues that may arise in prioritization, whereas the Proposed Revisions eliminate this opportunity for public input.

A more open and more detailed procedure enhances the final determination by facilitating the exchange of data and analyses. This phenomenon consistently was

recognized by OEHHA during the three years of drafting the Existing Procedure, which should be maintained.

OEHHA states that "workshops have been poorly attended and yielded few oral comments" as the basis for eliminating the workshop as an option in the prioritization process. (OEHHA, 2004b). The information that OEHHA does not share, however, is how many workshops have been requested but not conducted (there are several examples of this among our member companies), and the volume of the written comments received in conjunction with holding a workshop. OEHHA also claims that the Proposed Revisions still provide for two public comment opportunities, but this is not always true. The Proposed Revisions permit the Director to modify the process in any way, including eliminating one or both of the public comment opportunities. In contrast, the Existing Procedure provides that "appropriate notification periods will be followed" even when the Director modifies the process.

Finally, it appears that the Proposed Revisions resulted from several meetings of a SAB subcommittee in violation of California open meeting laws. (22 CCR § 12302(d)(1); Cal. Gov't Code § 11123). The failure to open the deliberative process to the public and the less open process proposed create an untenable basis for changing the current procedure.

IV. The Proposed Revisions Depart From Proposition 65's "Clearly Shown" Standard for Listing Chemicals

The core responsibility of the Identification Committees is to express their scientific opinions concerning whether certain chemicals have been "clearly shown" to cause cancer or reproductive toxicity. Proposition 65 provides:

"A chemical is known to the state to cause cancer or reproductive toxicity within the meaning of this chapter if in the opinion of the state's qualified experts it has been clearly shown through scientifically valid testing according to generally accepted principles to cause cancer or reproductive toxicity."

Cal. Health & Safety Code § 25249.8(b).

Neither the purpose of the Identification Committees nor the purpose of Proposition 65 is served by having the Identification Committees review chemicals that do not have a reasonably strong chance of meeting the statute's "clearly shown" standard. Thus, the Existing Procedure states "Chemicals will be assigned a high level of hazard concern if this preliminary evaluation indicates the existence of evidence that is likely to demonstrate a strong and biologically plausible potential to cause cancer or developmental/reproductive toxicity." The Proposed Revisions would remove this standard from the procedure and thus should be expected to provide less filtering of the chemicals reviewed by the Identification Committees than the Existing Procedure. The Identification Committees reviewed seven high priority chemicals during the prior four years, but only two of those seven were found to satisfy the clearly shown standard.[4] This low yield rate indicates that OEHHA should maintain or *increase* its standards for the level of toxicological evidence warranting submission to the Committees, not remove the standard entirely.

OEHHA claims that the Proposed Revisions respond to deficiencies noted by the CIC in December 2002. A review of the transcript for that meeting, however, does not support this claim. Instead, two members of the CIC, Drs. Hertz-Picciotto and Mack

[4] The Identification Committees reviewed a number of other chemicals during this period through OEHHA's procedure for referring certain chemicals considered by authoritative bodies. See 22 CCR § 12306(i).

requested that "some alternatives" be identified for later discussion; no vote of the CIC was taken. (CIC, 2002 at 172). The CIC never stated that the Prioritization Procedure should "better take into account the level of exposure and population potentially affected by various chemicals being reviewed by OEHHA, as well as the degree and extent of potential harm posed by the chemicals." (OEHHA, 2004a). The CIC members articulating the request for alternatives appeared to be under the mistaken impression that certain factors in the prioritization process were not taken into account at all. For example, Dr. Mack noted "there is information that would be useful to put into that [prioritization] process that you're not now doing perhaps." (CIC, 2002 at 173). Dr. Hertz-Picciotto said: "In light of what appears to be a process that is not not [sic] as effective in protecting public health as it could be, I would like to propose that we ask OEHHA to consider and bring before the committee some alternatives that would take into account toxicity/carcinogenicity data, exposure, and that means both level of exposure and population affected, and other relevant information to the seriousness of health effects that might be expected from exposure." (CIC, 2002 at 172). All of the factors cited by Dr. Hertz-Picciotto are considered in the current prioritization process.

The CIC's action in December 2002 also can not be interpreted as a request for exposure to play a greater role in the Prioritization Process. All three of the tasks on the CIC agenda for that meeting related to chemicals that OEHHA identified as high exposure chemicals and that OEHHA considered as warranting a high level of carcinogenicity concern. The CIC's request that the prioritization procedure be reevaluated can be seen as much as a reflection on the prioritization evaluations of OEHHA as a reflection on the prioritization process itself. The chemicals reviewed for

listing in December 2002 all were evaluated by OEHHA as having high exposure potential and high levels of carcinogenicity concern.

V. Prioritization Revisions Are Not an Effective Use of Resources

OEHHA deliberated upon the Existing Procedure for over three years. The record of those deliberations is replete with comments that OEHHA should utilize its resources to examine substance, not process. Now that sound procedures are in place for the prioritization of chemicals in a manner consistent with the statute, these comments are ever more apropos. There simply is no need for OEHHA to revise the existing prioritization process.

The Proposed Revisions provide for a less detailed, less thorough evaluation that does not allow for consideration of new information and automatically extrapolates animal data to humans. Thus, chemicals assigned a "high" priority pursuant to the Proposed Revisions would undergo the preparation of a Hazard Identification Document and would be reviewed by a Committee even if further analysis or subsequent information revealed that the chemical did not have a strong and biologically plausible potential to cause cancer or reproductive toxicity. This inevitable submission of high priority chemicals to the Identification Committees, regardless of the information that comes to light after the initial prioritization, will result in a waste of resources by "going through the motions" for chemicals that do not satisfy the statute's rigorous "clearly shown" standard. Furthermore, this waste of resources would appear to be a frequent risk because the Proposed Revisions specifically defer any review of complicated issues until after prioritization and eliminate the "tiered" evaluation approach of the Existing Procedure.

The Existing Procedure provides that OEHHA will spend less time on the prioritization of chemicals with straightforward toxicological evidence and more time on the chemicals that present more complicated issues: "[T]he level of analysis employed during the course of assigning final priorities will vary according to the complexity of the toxicological issues to be addressed. Preparation of a data summary will provide sufficient information for many chemicals, while for others, additional analysis supplemental to the data summary may be necessary to resolve particular scientific issues prior to the assignment of a final priority." (OEHHA, 1997). Since this time must be spent in the analysis of a chemical in any event before the chemical is presented to an Identification Committee, it makes sense to devote enough resources during the prioritization stage to confirm that a chemical truly warrants a "high" priority designation. To do otherwise inevitably will result in the analysis after the prioritization demonstrating that some (or many) chemicals do not warrant submission to the Identification Committee, with no prospect for saving staff and Committee time by avoiding that outcome.

VI. The Proposed Revisions Are Unnecessary

Proposition 65 now regulates over 750 different chemical exposures. This vast list of regulated chemicals is well beyond the number of chemicals envisioned to be covered by the law when it was passed. The original chair of the Scientific Advisory Panel, Dr. Wendell Kilgore, said in December 1987, "I expect that there will probably be approximately 300 compounds eventually on our list." (SAP, 1987 at 164). At this stage of Proposition 65 implementation, it should be expected that the high exposure chemicals with uncomplicated toxicological profiles already have been considered. The chemicals

that remain for possible evaluation warrant the more rigorous evaluation called for by the Existing Procedure, not the less thorough approach in the Proposed Revisions.

VII. The Proposed Revisions Contradict Prior Expert Panel Input

The Proposed Revisions contemplate review of draft prioritization decisions by the Carcinogen Identification Committee, with public comment. The Carcinogen Identification Committee unanimously rejected this proposal in 1996. This unexplained, total reversal of approach reveals that the Proposed Revisions do not account properly for the substantial Committee and public comments that were dedicated to prioritization issues from 1994 through 1996.

The July 1996 meeting agenda for the CIC included that Committee's approval of draft priorities assigned by OEHHA for various chemicals. The Committee unanimously refused to do so. The OEHHA Director asked: "Does the Committee concur with the priorities that have been assigned at this time?" (CIC, 1996 at 67). Chairman Mack responded:

> "I'm going to rephrase that question. The question really is: Does the Committee want to get into a discussion of the relative merits of individual chemicals in the prioritization process?
>
> "I, obviously, rephrase it that way because it's a fairly significant decision if we wanted to do that. It would be a substantial commitment of time, particularly since there is going to be no prioritization which makes everybody happy. I would dare say that doesn't just refer to the stakeholder community. It refers even to the Committee.

"These are arbitrary judgments and they're going to be contentious, so it would mean a substantial commitment of time in reviewing data, which is going to have to be reviewed anyway when we get hazard documents."

(CIC, 1996 at 67-68).

Dr. Peters, another member of the CIC, immediately concurred:

"It was my understanding that we had been constituted to review the scientific processes that were gone through and to make sure that they made scientific sense, at least to us.

"And that, in pursuit of that, we would be reviewing work done by the State in preparing things for making decisions, but that being involved in specific individual chemicals from the, you know, grassroots up was not a role that I thought was meant for us, nor one that I want."

(CIC, 1996 at 68).

The discussion concluded with a unanimous indication from the Committee that it did not want to be involved in reviewing prioritization determinations, that was OEHHA's role:

"CHAIRMAN MACK: Anybody else wish to address the issue?

"Are we unanimous then in wishing not to get into individual chemical considerations in the prioritization process? All right. I would not think a motion is required.

"Next question."

(CIC, 1996 at 68-69).

VIII. Conclusion

For the reasons described above, OEHHA should withdraw or take no action on the "Update – September 2004 Draft" prioritization process document. OEHHA should maintain the May 1997 Prioritization Procedure that was duly adopted after extensive public comment and public hearing.

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