

**RESPONSES TO COMMENTS SUBMITTED BY THE CHLORINE
CHEMISTRY COUNCIL**

Comment 1: OEHHA should not assign dioxin to Tier 1 without first determining whether dioxin air emissions in California contribute significantly to childhood exposures.

The Draft document should assign higher priority to chemicals for which Californian air emissions are a primary source of exposure. The primary source of human dioxin exposure is through the diet. Any exposure through inhalation is negligible. Indeed, over 95% of a person's daily exposure to dioxin is due to dietary intake, primarily from meat, fish and dairy products.

Although exposure to dioxin by inhalation of ambient air is relatively insignificant, air deposition of dioxin is thought to be a significant route for food contamination. Air, therefore, may be a significant source of dioxin exposure to children in California, albeit through an indirect route. However, given that food consumed by Californians may come from anywhere in the world, a question arises as to whether dioxin air emissions in California substantially affects food consumed in California. Further, given that dioxin may be transported over long distances (typically across state lines), to the extent Californians consume dioxin contaminated food originating in California, a question arises as to whether the dioxin originated in California.

OEHHA may find that the majority of dioxin in Californian is attributable to emissions outside of the State (either dioxin contaminated food originated outside of the State or the air emission source is located outside of California) - emissions that California cannot control. In that event, dioxin should be assigned a lower priority to allow higher priorities for chemicals for which the State can control exposures.

Response: In its draft document, OEHHA acknowledged that ingestion is the main route of exposure to dioxin and dioxin-like chemicals. It also recognized that dioxins and

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related persistent chlorinated pollutants are present in all media including sediment, soil and biota, and that they are likely to be recirculated into the atmosphere. There are, however, documented emission of dioxins and benzofurans in California. As reported in the California Air Resources Board (CARB) report¹ cited in OEHHA's draft document, Los Angeles region, for instance, was responsible for the release of 58 lb of dioxins and benzofurans per year. Other regions in California, although to a lesser extent, also contributed to dioxins and benzofurans release as reported in the ARB's 1996 California Toxics Inventory (revised 8/28/00). Dioxins are initially airborne, deposit on food and feed and enter the food chain. Controlling airborne sources thus reduces overall exposures. Therefore, OEHHA has assigned dioxin a TAC priority level based on the overall importance of airborne dioxin, including consideration of exposure levels in food. The present stage of the process is concerned with prioritizing TACs for further evaluation, based primarily on toxicity information and on evidence for current exposures in California. Data on specific sources of the materials or trends in emissions will undoubtedly be of great interest to the California Air Resources Board if they reconsider the requirements for Air Toxics Control Measures.

Comment 2: OEHHA should factor into its prioritization the significant reduction in the levels of dioxins along with the recognition that these declines are expected to continue

New technologies, as well as actions by both government and industry have been successful in significantly reducing the level of dioxin in the environment. Major dioxin reductions have been and will continue to be achieved. The U.S. Environmental Protection Agency (EPA) data indicate that US dioxin emissions were slashed by 75% from known sources between 1987 and 1995. Furthermore, according to EPA, strict new regulatory standards and technologies affecting municipal, medical, and hazardous waste incinerators will reduce emissions from these sources by 90-95%.

¹ Air Resources Board (ARB, 2000). California Ambient Toxics Monitoring Network. <http://www.arb.ca.gov>.

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Prior to placing dioxin in Tier I, OEHHA should determine whether, given the significant controls on and reductions in dioxin emissions, significant further reductions in dioxin air emissions can be accomplished. OEHHA may find that future dioxin exposures may result from un-controllable sources, possibly existing dioxins recirculating in the environment. In that event, OEHHA should assign dioxin a lower priority to allow greater attention and expenditure of limited resources on chemicals for which air emissions and exposures can be effectively controlled.

Response: As reported in its draft document, OEHHA is aware of the past reduction in dioxin emissions partly attributable to regulatory standards targeting municipal combustors and medical incinerators. We are also aware of and applaud the efforts of the paper industry to reduce dioxin formation during chlorine bleaching of pulp. However, dioxins and related persistent chlorinated pollutants are present in all media including sediment, soil and biota, and are likely to be recirculated into the atmosphere. Because of their persistent and bioaccumulative properties, dioxins originally released into the air are found in all levels of the food chain, including humans. Therefore airborne dioxins (from anthropogenic or natural sources) are environmental contaminants that still require close attention.

Comment 3: The OEHHA Draft Appendix inappropriately groups several classes of chemicals together.

The scientific literature from animal studies demonstrates clearly that different PCB compounds have qualitatively different effects on the neurodevelopmental endpoints cited by OEHHA as being of concern; this is acknowledged by OEHHA on pp. 12-13. Further, the animal literature also indicates that dioxin and furan compounds have little effect on neurodevelopmental endpoints, and where effects have been observed, they may indicate improved functioning in exposed animals (Tilson and Kodavanti, 1998, as cited in OEHHA, 2001). As discussed below, interpretation of the human literature is difficult due to problem with exposure assessment and study design. However, even this literature indicates that effects cannot be directly linked to summed or grouped exposure to

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polychlorinated dioxins, furans, and biphenyls. OEHHA (2001) also acknowledges that different subclasses of these compounds may have different mechanisms of action.

Grouping compounds that do not share similar effects or mechanism of action is inappropriate. Finally, even among sub-groups of these compounds believed to have similar effects and to operate via a similar mechanism of action, the potency of these compounds varies widely.

Response: OEHHA appreciates the comment on the different effects of various classes of PCBs. It was precisely the goal of this draft document to provide an up-to-date report of the current knowledge about dioxin and related chemicals. So, as noted in this comment and reported in our draft document, PCB toxicity occurs through at least two pathways. The toxicity of co-planar and partially co-planar PCBs (which are often referred to as dioxin-like compounds) occurs through binding of the Ah receptor (AhR), similar to TCDD. The second mechanism of toxicity involves non-coplanar PCBs (di-ortho, and some mono-ortho PCBs), and is reported to interfere with calcium homeostatic mechanisms and intracellular second messenger systems *in vitro* in neuronal cultures and brain subcellular fractions (Tilson and Kodavanti, 1998)². The *in vivo* mechanism of developmental neurotoxicity for this type of PCBs is not clearly established. In the specific case of non-planar PCBs, OEHHA agrees that, for these chemicals, the scheme of TEQ calculation used for dioxin-like compounds cannot be applied since they exert their toxicity through a mechanism different than the TCDD/AhR pathway. Nevertheless, two chemicals with different mechanism of toxicity may adversely affect the same target. For the chemicals operating through the AhR, the TEQ calculation scheme is well documented and accepted by several agencies including USEPA. In addition, the neurodevelopmental as well as the immunological and hormonal effects represent well-documented endpoints attributable to dioxins and related chemicals. Dioxins, furans and PCBs share similar fate in the environment and in most cases share the AhR pathway of toxicity. OEHHA considered non-coplanar PCBs in a separate specific group.

² Tilson, H. A., and Kodavanti, P. R. S. (1998). The neurotoxicity of polychlorinated biphenyls. *Neurotoxicology* **19**, 517-526.

Comment 4: The introductory section and the conclusions of the report overstate or misrepresent the literature cited in the main body of the report. The document should present the most accurate depiction of the potential threats associated with dioxin in order to ensure that California focuses on priority public health concerns and avoids the unintended consequences of overstating potential risk.

The main body of the report summarizes findings from a variety of animal and human studies without attempting to critically assess the strengths of the studies or provide a critical assessment of the consistency of the findings among studies. In the summary of the human literature on developmental endpoints, the document does not discuss the many issues critical to the interpretation of these studies. For example, in the presentation of data from studies of the Dutch population, none of the following critical issues are mentioned or discussed:

These studies consist of mother-infant pair from two different areas of the Netherlands, and key demographic factors known to influence infant development are substantially different between the two groups. These studies assess a variety of exposure indices (perinatal vs. postnatal; summed PCBs vs. TCDD toxic equivalents, or TEQs) and a multitude of endpoints. Findings are sporadic and not consistent from one time period to another, and vary depending on exposure measure. Findings in relationship to exposure indices are different in formula-fed and breast-fed infants. Reported variations in developmental endpoints are subtle and within the range of normal variability. The researchers acknowledge that their findings are more pronounced in the formula-fed infants, even though the breast fed infants experienced doses of dioxins, furans, and PCBs of four to six times higher.

A careful reading of the Dutch studies demonstrates that the only truly consistent and reliable conclusion that can be drawn from these studies is that breast feeding produces better neurodevelopmental outcomes than formula feeding. This important public health

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message is obscured by the recitation of findings without context is the OEHHA document.

Response: OEHHA's draft document presents several experimental epidemiological studies from which the conclusive outcomes might appear to be contradictory. OEHHA concedes that a restricted reading of some citations would seem to indicate that there is no threat posed by dioxin. However, when considering the whole document, the trend is clear, background level of dioxins and related chemicals cause detrimental effects in children for all sensitive endpoints selected. For the Dutch study³ comment, OEHHA's document clearly reports on page 9 that breast-feeding was not significantly associated with reduced growth for the first 3 months. However, in utero exposure to PCBs was associated with reduced growth for the first three months.

Comment 5: Inaccuracies in the section Summary of potential for differential effects (page 5) highlight the lack of a critical appraisal of the data included in the report. This section cites in broad scope the basis for OEHHA's determination that there is a potential for differential sensitivity in children to the effects of dioxins, furans, and PCBs. The third sentence in this paragraph is a garbled quote from the source cited, Feeley and Brouwer (2000). The sentence in Feeley and Brouwer (2000) is designed to support the conclusion that TCDD and related compounds are transferred to the fetus. The entire relevant quote is as follows:

“Human fetuses of 8-14 week gestational age (elective abortions) have been analyzed for PCDDs/DFs and found to contain approximately 30% of the TCDD TEQ of human milk (5.3 ng/kg lipid vs. 16.7 ng/kg lipid) (Schechter et al. 1996a).”

³ Patandin, S., Koopman-Esseboom, C., de Ridder, M. A., Weisglas-Kuperus, N., and Sauer, P. J. (1998). Effects of environmental exposure to polychlorinated biphenyls and dioxins on birth size and growth in Dutch children. *Pediatr Res* **44**, 538-45.

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Response: OEHHA thanks the commenter for pointing this out. The quotation will be corrected in the final report. As noted in the comment, this sentence illustrates the transfer of dioxin from the mother to her fetus, and thus the fetus can experience early exposure to chlorinated contaminants.

Comment 6: The next sentence of the OEHHA document cites non-specific "functional developmental effects" observed in the rice oil poisonings. The children studied from this episode were offspring of mothers that suffered frank poisoning with exposure levels several hundred times background levels. These children have demonstrated a range of short-term and longer-term effects. However, the following sentence says that " similar effects were also observed in children as a result of background exposure to these chemicals." The cited articles do not clearly support that statement. Papke (1998) does not present data on any type of developmental effect; rather, it presents data showing that background exposure levels to PCDDs/DFs have been steadily declining. The findings of Gladen et al. (2000) are not similar to those reported in the rice oil poisoning incidents, as the researchers found essentially no relationship between their assessment of perinatal exposure to PCBs (a flawed exposure assessment) and body size at puberty. Similarly, the study of Vartiainen et al. (1998) was essentially negative, with no meaningful correlation found between exposure to dioxins and birth weight, sex ratio, or other developmental endpoints. The findings presented in the other cited studies were of various subtle endpoints not directly comparable to the frank manifestations reported in the rice oil poisoning incidents. The reported findings in these papers are subtle, often conflicting and are not interpretable as consistent evidence of adverse effects in children exposed to background levels.

Response: OEHHA must respectfully disagree with this comment. All of the cited references present evidence of subtle but significant adverse effects associated with exposure to dioxins and related chemicals. These effects extend from decreased growth to cognitive retardation. Some of the effects observed in children born to mothers exposed to the contaminated rice-oil in Yu-Cheng are similar to those observed in

children after *in utero* exposure to background level of dioxin and related chemicals. The Papke (1998)⁴ citation is provided to give a reference to background level of dioxins and related chemicals. Gladen et al. (2000)⁵ reported that prenatal exposures at background levels to PCB affects body size at puberty in girls. In Vartiainen et al. (1998)⁶ the birth weight, especially of boys, slightly decreased with increasing concentrations of I-TEQ, 2,3,4,7,8-pentachlorodibenzofuran, 1,2,3,7,8- pentachlorodibenzodioxin, and 2,3,7,8-tetrachlorodibenzodioxin in mother's milk. All of these papers are included in the body of the report and objectively presented.

Comment 7: The tone of the Conclusions section of the report (p. 19) is overly conclusive. The document presents no critical evaluation of the human studies that are the primary basis for the conclusions. Among the issues not discussed in the document are the many inconsistencies in findings among different studies, the problems associated with exposure assessment, and the lack of adequate control for potential confounding factors in many of the cited studies. However, the affirmative tone of the conclusion gives the impression that the results of the studies are unambiguous and unarguable.

The final paragraph asserts that "current background levels of exposure to dioxin in particular are within the range at which various toxic responses have been observed in animals." This statement is not strictly true, and no quantitative data are presented to support this statement.

⁴ Papke, O. (1998). PCDD/PCDF: human background data for Germany, a 10-year experience. *Environ Health Perspect* **106 Suppl 2**, 723-31.

⁵ Gladen, B. C., Ragan, N. B., and Rogan, W. J. (2000). Pubertal growth and development and prenatal and lactational exposure to polychlorinated biphenyls and dichlorodiphenyl dichloroethene. *Journal of Pediatrics* **136**, 490-496.

⁶ Vartiainen, T., Jaakkola, J. J., Saarikoski, S., and Tuomisto, J. (1998). Birth weight and sex of children and the correlation to the body burden of PCDDs/PCDFs and PCBs of the mother. *Environ Health Perspect* **106**, 61-6.

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Response: OEHHA's conclusions are based on all studies presented in its report.

Although some studies present negative results, as a whole, the data cited in OEHHA's document indicate that there is an increasing number of reports demonstrating a link between background level of dioxins, and related chemicals and adverse immunological, neurobehavioral and developmental effects in infants and children. This trend seems to be increasing in the newly published literature.

Comment 8: OEHHA must strive to present a scientifically sound, critical appraisal of the relevant data. It is imperative that OEHHA accurately portrays the scientific evidence regarding potential risks associated with background exposures to polychlorinated dioxins, furans, and biphenyls. This is critical to ensure that the state focuses its limited resources on priority public health issues and avoids overestimating potential risks, which could inadvertently result in negative consequences for public health. Such inadvertent consequences could include a shift away from breast-feeding or, a decline in balanced diets.

Response: OEHHA's draft document presents an objective review of the scientific literature describing the potential risks associated with background exposures to polychlorinated dioxins, furans, and biphenyls. The objective of OEHHA is not to discourage breast-feeding or ban certain foods. On the contrary, our main goal is to promote regulatory measures that identify and control environmental and food chain contamination.

Comment 9: OEHHA should recognize in its prioritization the significant scientific uncertainty regarding dioxins and should therefore delay a final ranking of dioxins until EPA has released its Dioxin Reassessment.

There currently exists a significant amount of scientific debate and disagreement concerning the risks posed by dioxin. Indeed, EPA has been attempting to reassess the toxicity of dioxin over the last ten years. Delays in finalizing a dioxin reassessment have

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been due to the deep disagreement of well respected scientists (including EPA's own peer reviewers) concerning the quality of the science on dioxin, the conclusions that can be drawn from that information and the uncertainty surrounding risk estimates related to potential dioxin exposures. Therefore OEHHA should delay a final ranking of dioxin until EPA has released its Dioxin Reassessment.

Response: OEHHA is aware of the uncertainty surrounding some aspects of dioxin toxicity. We are familiar with the US EPA's draft report on dioxin and related compounds, and their inventory calculations. We also await with interest measurements currently being made or planned by US EPA. However, the OEHHA draft report is a hazard identification document, not a risk assessment. There are plenty of studies indicating concerns for the impacts of dioxin exposures on infants and children.

Comment 10: OEHHA failed to demonstrate that children are especially susceptible to dioxin.

Pursuant to the Children's Environmental Health Protection Act, OEHHA is required to develop a list of TACs that may cause infants and children to be especially susceptible to illness. The Draft Document fails, however, to demonstrate that children and infants are especially susceptible to dioxin. Although some have speculated that developing children may be more sensitive to dioxin exposures, the scientific evidence does not substantiate the claim nor does evidence clearly refute the claim. Nonetheless, it is interesting to note (as discussed above) that breast-fed children, who ingest relatively high doses of dioxin, have been shown to have better outcomes in certain developmental parameters than bottle-fed infants.

Response: Increased susceptibility of the developing fetus/infants to environmental contaminants is attributed to both the inherent vulnerability of the developing organ system and the timing and extent of exposure (Feeley and Brouwer, 2000)⁷. In addition,

⁷ Feeley, M., and Brouwer, A. (2000). Health risks to infants from exposure to PCBs, PCDDs and PCDFs. *Food Addit Contam* **17**, 325-33.

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children are particularly susceptible to exposure to contaminated soil or dust because of the mouthing habit often seen in infants and young children. From its review of the literature, OEHHA believes that background level of dioxins and related chemicals represent a potential threat to developing fetuses and infants. Therefore, this family of chemicals substances should be monitored closely.

OEHHA agrees with the comment on breast-feeding; the beneficial properties of breast milk are confirmed in many instances. OEHHA, however, strongly disagrees with the limited interpretation of this statement. The study cited in the draft report (Boersma et al., 2000) suggested that although breast-fed infants had significantly higher levels of dioxin compared to formula-fed infants, despite this high dioxin intake, breast-fed infants showed less adverse cognitive and neurological effects attributable to dioxin and PCB exposures than did those children exposed *in utero* but formula-fed as infants. Infants exposed *in utero* who were formula-fed did not have the benefit of breast-feeding and were more adversely affected than the control group and than the exposed group who were breast-fed.. This demonstrates the positive impacts of breast-feeding and not a lack of effect of *in utero* exposure to PCDD/F and PCB.

Comment 11: Children have been shown to be especially susceptible to certain substances, such as lead and mercury. Clearly, efforts should be made to limit childhood exposures to such substances. To that effect, care should be taken not to unnecessarily draw resources away from managing exposures to substances known to pose such unique hazards to children. To avoid such a result, OEHHA should not place a substance in Tier 1 until it has determined that children are especially susceptible to the substance. Indeed this is precisely what the Act appears to require.

Response: OEHHA in its prioritization process has considered hundred of chemicals substances and came up with a short list of eleven chemicals. The selection of these chemicals, and the prioritization of the five chemicals that were included in the Tier 1

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was based on evidence reviewed in the scientific literature. Strategies for appropriate direction of effort in controlling these hazards are the responsibility of the California Air Resources Board, and we defer to them with regard to the allocation of resources in revising or augmenting its Air Toxics Control Measures.