February 1, 2002

Joan Denton, Ph.D.
Director
Office of Environmental Health Hazard Assessment
California Environmental Protection Agency
1001 I Street
Sacramento, California 95814

Dear Dr. Denton:

With this letter I am pleased to transmit the findings of the Scientific Review Panel (SRP) which are based on our review of the Office of Environmental Health Hazard Assessment (OEHHA) report "Prioritization of Toxic Air Contaminants under the Children's Environmental Health Protection Act."

OEHHA is required by the Children's Environmental Health Protection Act (SB 25) to establish a list of up to five toxic air contaminants "that may cause infants and children to be especially susceptible to illness." The Panel has concluded the OEHHA report that lists: acrolein, particulate emissions from diesel-fueled engines, chlorinated dioxins and dibenzofurans, lead and lead compounds (organic and inorganic), and polycyclic organic matter is based on sound science and reflects a thorough review of the scientific literature.

The subject of the identification of chemicals that may have differential susceptibility between adults and children is difficult because there is a limited database that has focused on the issue. Your staff and the Panel had to grapple with evaluating chemicals having multiple endpoints, such as carcinogenicity, developmental and neurological toxicity and allergic airway disease including asthma. Based on our review of the report the Panel determined there were other chemicals of concern that require follow up over time. We would encourage OEHHA to discuss the overall issue of differential susceptibility further with the National Institute of Environmental Health Sciences in order to develop a coordinated effort on the topic.

We appreciate the considerable efforts of OEHHA's scientists in the report development and their participation in responding to the Panel's concerns. The Panel recognizes this report represents a major effort on the part of OEHHA and is a unique document in meeting the requirements of SB25. If the Panel may be of further help in addressing children's health, we would be pleased to do so.

Sincerely,

s/

John R. Froines, Ph.D.
Chairperson
Scientific Review Panel

Enclosure

cc: Alan C. Lloyd, Ph.D.
Chairman
Air Resources Board

Paul E. Helliker
Director
Department of Pesticide Regulation

Findings of the Scientific Review Panel on
Prioritization of Toxic Air Contaminants Under the Children's Environmental Health Protection Act
as adopted at the Panel's November 28, 2001 Meeting

Pursuant to California Health and Safety Code section 39669.5(a)(2), the Scientific Review Panel (SRP/Panel) has reviewed the report *Prioritization of Toxic Air Contaminants Under the Children's Environmental Health Protection Act* by the staff of the Office of Environmental Health Hazard Assessment (OEHHA) describing the process of prioritizing Toxic Air Contaminants (TACs) for listing under the Act, and including summaries of the toxicity of TACs that were considered for the initial list of up to five TACs that may cause infants and children to be especially susceptible to illness. The Panel members also reviewed the public comments received on this report.

OEHHA is required by law (Health and Safety Code section 39669.5.(a)(1)) to establish a list by July 1, 2001of up to five toxic air contaminants "that may cause infants and children to be especially susceptible to illness".

Panel members participated in extensive discussions at public meetings on this report, held on April 27, May 14, June 15, and July 30, 2001. Based on discussions at the meetings and review

of the document, the SRP makes the following findings pursuant to Health and Safety Code sections 39661 and 39669.5:

Findings Related to Disproportionate Impacts on Children of Toxic Air Contaminants

1. Few scientific studies specifically address age-dependent differential susceptibility to air toxics. For several TACs, there is a developed literature on health effects in children and/or young laboratory animals, but the available studies do not necessarily provide a basis for comparison to adult toxicity. These data gaps pose the single largest obstacle to defining health risks to infants and children as specified by SB25.

2. In the absence of adequate data to determine differential health consequences of exposure to infants and children relative to adults, potentially important compounds were identified in part by their association with toxic endpoints that have greater consequence for young organisms. General classes of toxic effects known to have more impact on young, developing organisms include neurotoxicity, immunotoxicity and respiratory toxicity, including irritation and effects on asthma. Fetal damage sustained as a result of exposure to environmental toxicants is a source of adverse postnatal health impacts, and therefore developmental toxicity is also an endpoint of concern for infants' and children's health. The Panel concluded that, given the significant problems with the database on TACs for infants and children, it is scientifically reasonable to consider production of one of these types of toxicity as an indicator of potential concern.

3. The panel agrees with OEHHA that exposures to carcinogens early in life may result in a greater lifetime risk of cancer. In addition, childhood cancer incidence has been rising in recent decades. Therefore carcinogens to which children have particularly high exposures require careful examination.

4. Selection of top candidate TACs under SB25 was based not only on evidence of toxicity relevant to infants and children, but also on exposure levels and the potential for infants and children to receive disproportionately large doses in comparison to adults. Available ambient air concentrations and California emissions data were used by OEHHA to provide general characterization of population exposure levels. Panel members noted that characterization of exposure levels was quite difficult because data on ambient air concentrations was lacking for a substantial fraction of TACs. In addition, local air concentrations of TACs in the vicinity of emissions "hot spots" is lacking, yet locally high exposures may pose considerable risks.

   Given a particular air concentration, infants and children receive higher doses of TACs via inhalation than adults due to greater breathing rates. In addition, infants and children may be more highly exposed than adults because of exposure scenarios unique to them that result in greater contact with toxicants. Examples include ingestion of air-borne toxicants via breast milk, or after deposition onto food and soils. Evidence of disproportionate exposure was an important factor in selecting TACs for listing under SB25.

5. OEHHA employed a step-wise approach to identifying the top five TAC candidates for evaluation. Available data on ambient air concentrations and health assessment values, including Reference Exposure Levels and Unit Risk Factors, were gathered for all TACs and

used for ranking risks at a screening level. Using these rankings, plus California emissions data and knowledge of toxic effects that pose a potentially greater impact on developing organisms, OEHHA selected 37 TACs for literature reviews. OEHHA, responding to Panel feedback, identified 17 TACs that may cause infants and children to be especially susceptible to toxicity and which were candidates for the first group of five to be listed. Summaries of exposure and toxicity data pertinent to children's health risks for these TACs are found in Appendices C1 and C2 of OEHHA's document. To select the top priority compounds, epidemiological and toxicological data indicating differential toxicity and adverse consequences for infants and children relative to adults was weighted heavily. Indication of potentially high exposures, either from ambient air or from localized sources of emissions provided a second axis of priority weighting. Thus, extensive exposure was a key criterion for some of the top candidates, while for others low exposures were offset by considerable toxicological concern.

6. The Panel agrees with OEHHA that the following five TACs should receive the first priority under SB25: acrolein, particulate emissions from diesel-fueled engines, chlorinated dioxins and dibenzofurans (hereinafter referred to as dioxins), lead and lead compounds (organic and inorganic), and polycyclic organic matter. The specific rationale for listing each of these compounds or groups of compounds is given in Findings 7-11. The health effects discussed are those pertinent to SB25; all of the health effects associated with each specific chemical are not necessarily discussed. For example, carcinogenesis in adults may be associated with one or more compounds, but might not be discussed in these Findings.

7. **Acrolein** was selected as a Tier 1 priority substance based on its potential to exacerbate asthma and because current exposure levels are a concern. *In vivo* and *in vitro* data in animals and *in vitro* data using human tissue document changes in epithelial tissue associated with asthma. Children have higher prevalence rates of asthma, and their smaller airways predispose to more severe consequences of asthma attacks than adults. The increase in severity of asthma episodes especially affects very young children. Thus, on a population-wide basis, exacerbation of asthma by acrolein in the air results in disproportionate impacts on children. Acrolein is also a potent irritant and a strong electrophile, with potential for macromolecular binding. While uncertainty exists in quantifying exposure, measurements and models of acrolein concentrations in ambient air indicate that the general population is exposed to significant concentrations of acrolein which are at or above the chronic Reference Exposure Level. These observations indicate that children are disproportionately impacted by exposure to acrolein, and, therefore, acrolein should be listed by OEHHA as a TAC which may cause infants and children to be especially susceptible to illness.

8. **Diesel exhaust particulate (DEP)** was selected as a Tier 1 priority substance based primarily on widespread exposure and data indicating enhancement of allergic responses and other adverse respiratory symptoms in both experimental and epidemiological studies. A variety of experimental studies in humans and animals have shown that DEP acts as an adjuvant in allergic and inflammatory responses. DEP may exacerbate allergic airway disease including asthma. A possible role in induction of atopy and asthma is indicated by data showing that DEP can facilitate the development of new allergy to airborne allergens. Asthma impacts children disproportionately relative to adults, as discussed in Finding 5 on acrolein. Several

epidemiological studies have reported associations between truck traffic density (largely diesel-powered) and adverse respiratory symptoms, including atopy, in children living along busy roadways. In one of these studies, children were more impacted by traffic-related pollutants than adults in the same household. Finally, DEP contains POM, which was also placed in Tier 1 for listing under SB25 (see finding #11). Due to their higher breathing rates and smaller airways, children are exposed to more particulate per lung surface area than adults in the same environmental setting. Together, these observations indicate that children are disproportionately impacted by diesel exhaust particulate, and therefore diesel exhaust particulate should be listed by OEHHA as a TAC which may cause infants and children to be especially susceptible to illness.

9. **Dioxins** and related compounds were selected as Tier 1 priority substances based on a wide spectrum of toxic effects including endpoints that are of particular concern for infants and children. Although current air concentrations are low, the majority of exposure is still thought to originate with air emissions. There is evidence in humans and laboratory animals for immunotoxicity. Endocrine toxicity, including altered reproductive development, has been documented in humans and laboratory animals. While there are not specific data to indicate that children are more susceptible to experiencing these effects, immune and endocrine toxicity has a greater impact on the lifetime health of young and developing organisms, and effects that are reversible in adults may be irreversible when they occur in the young. Dioxins also induce developmental toxicity including low birth weight (humans) and teratogenicity (animals). Children receive greater exposures to dioxins than adults in similar settings, and in particular, breast-fed infants receive about 50 times more dioxins on a body weight basis per day than adults. The range of toxic effects observed indicate that children are disproportionately impacted by exposure to dioxins, and therefore dioxins should be listed by OEHHA as a TAC which may cause infants and children to be especially susceptible to illness.

10. **Lead** was selected as a Tier 1 priority toxic air contaminant based on a substantial body of epidemiologic and laboratory experimental data documenting neurotoxicity. The large database on lead demonstrates that developing organisms are the most susceptible population to the neurotoxic effects of lead. Although lead levels in air have dropped dramatically since the ban on lead in gasoline, considerable emissions from stationary sources still occur in California. Children are exposed to higher concentrations of lead than adults primarily due to hand-to-mouth activity and consequent ingestion of lead in dust and soil. These observations indicate that children are disproportionately impacted by exposure to lead, and, therefore, lead should be listed by OEHHA as a TAC which may cause infants and children to be especially susceptible to illness.

11. **Polycyclic Organic Matter** (including, but not limited to the following polycyclic aromatic hydrocarbons (PAH) and PAH derivatives: benzo[*a*]pyrene, benzo[*a*]anthracene, benzo[*b*]fluoranthene, benzo[*j*]fluoranthene, benzo[*k*]fluoranthene, dibenz[*a,j*]acridine, dibenz[*a,h*]acridine, 7H-dibenzo[*c,g*]carbazole, dibenzo[*a,e*]pyrene, dibenzo[*a,h*]pyrene, dibenzo[*a,i*]pyrene, dibenzo[*a,l*]pyrene, fluoranthene, 2-methyl fluoranthene, 3-methyl fluoranthene, indeno[1,2,3-*cd*]pyrene, 5-methylchrysene, naphthalene, 1-nitropyrene, 4-nitropyrene, 1,6-dinitropyrene, 1,8-dinitropyrene, 6-nitrocrysene, 2-nitrofluorene, chrysene, dibenz[*a*,h]anthracene, 7,12-dimethylbenzanthracene, 3-methylcholanthrene,

5-nitroacenaphthene) POM was prioritized in Tier 1 primarily because of adverse effects on birth weight, the immune system, the reproductive system and cancer resulting from fetal exposure. Reduced birth weight has been observed in animals exposed to specific PAHs, and associated with PAHs in air pollution in human epidemiological studies. Animal studies have shown teratogenic properties of some PAHs. Exposure to benzo[*a*]pyrene in *utero* caused a loss of fertility in adult mice. A comparative study of carcinogenic potency of benzo[*a*]pyrene indicated a shorter latency and higher tumor yield with earlier in life exposures. Transplacental carcinogenesis has been documented for PAHs. Children can have greater exposures than adults in the same setting, and indoor exposures are particularly high and relevant for children. The body of evidence as a whole indicates that children are disproportionately impacted by exposure to POM and specific components of POM and therefore POM should be listed by OEHHA as a TAC that may cause infants and children to be especially susceptible to illness.

Recent studies have shown that the PAH naphthalene damages ciliated and Clara cells of the bronchiolar epithelium and that neonatal mice are more sensitive to this effect than adult mice. In addition, naphthalene at high doses induces methemoglobinemia, an effect to which infants would be more sensitive than adults. Panel members noted that exposure levels may be higher for naphthalene than for other PAHs and this compound deserves special attention.

12. More generally, the Panel noted that the TACs diesel exhaust particulate, dioxins, and POM are complex mixtures comprised of many components. The TAC designation pertains to the mixtures rather than specific mixture components. The Panel is limited to recommending listing of designated TACs. However, Panel members were concerned that some components of these mixtures may be of particular concern to infants and children and that control measures for groups of compounds do not necessarily adequately address each component substance. Important examples include naphthalene and nitro-PAHs, the control of which are complex problems.

13. The Panel also finds that there are other toxic air contaminants of concern for infants and children but that the constraint of identifying up to five in the first Tier does not allow OEHHA to list these important toxic air contaminants at this time. The Panel recommends that the following compounds should be given high priority for future consideration under SB 25, for reasons summarized briefly in the table below: **arsenic, benzene, carbon disulfide, chlorine, ethylene glycol ethers, formaldehyde, manganese, mercury, methyl bromide, methylene chloride, non-coplanar PCBs, vinyl chloride**. ARB should continue to monitor emissions and air concentrations of all of these substances, and if locally high concentrations are identified through modeling or monitoring, OEHHA should consider listing them.

Compound	Rationale/comments
Arsenic	Known human carcinogen based on epidemiologic data on lung cancer, experimental data indicate developmental toxicity; generally low exposure.
Benzene	Known human carcinogen with concerns for childhood leukemia risks; considerable

	exposure concern.
Carbon disulfide	Occupational neurotoxicity, age-related differential metabolism; low emissions
Chlorine	Potent irritant; possible high concentrations at hot spots.
Ethylene glycol ethers	Developmental toxicity and localized high emissions
Formaldehyde	Respiratory toxicant with possible asthma exacerbation, some evidence of increased sensitivity in children; high ambient exposures
Manganese	Neurotoxicity in humans and animals, some evidence of increased sensitivity in young animals; currently, exposure is low.
Mercury	Clear evidence of developmental neurotoxicity; ambient air exposures very low.
Methyl bromide	Neurotoxic in humans and animals, some experimental evidence of teratogenicity; not a ubiquitous air pollutant, but indication of local high exposures.
Methylene chloride	Metabolized to CO, to which infants are more susceptible; very high hot spots emissions.
Non-coplanar and coplanar polychlorinated biphenyls (PCBs)	Coplanar PCBs have many effects in common with dioxins. Non-coplanar PCBs are developmental neurotoxicants. Current air emissions of both are very low.
Vinyl chloride	Known human carcinogen, with increased potency when administered to neonatal animals. Ambient exposures are very low.

14. **Environmental tobacco smoke (ETS)** is associated with substantial adverse health effects in infants and children including reduced birth weight, intrauterine growth retardation, increased risk of sudden infant death syndrome, exacerbation of asthma and induction of new asthma, chronic respiratory symptoms, increased lower airway infections, and acute and chronic otitis media. The health effects of ETS in children have a substantial public health impact in California. Since ETS has not been identified as a Toxic Air Contaminant, OEHHA is precluded from listing it under SB 25 at this time, despite the scientific evidence that ETS causes infants and children to be especially susceptible to illness. This Panel recommends that ETS be listed as a TAC, and the considerations for protection of infants and children required by SB25 be addressed at that time.

15. OEHHA is precluded by law from evaluating "pesticides in their pesticidal use" for listing under SB 25. There are several pesticides that are TACs and whose mechanism of toxicity (e.g., neurotoxicity) would suggest consideration for listing. However, SB 25 reiterated and confirmed previous statutory provisions specifying that pesticides in their pesticidal use are outside the purview of OEHHA and ARB in administering the Toxic Air Contaminant Program (Health and Safety Code Sections 39655 and 39660) One exception is methyl

bromide, noted in Finding 13 above, which an appellate court decision held may be regulated as an emission from fumigation chambers. There is a parallel component of the Toxic Air Contaminant Program under which the Department of Pesticide Regulation identifies pesticides as TACs. The Panel recommends that parallel or similar consideration of infants' and children's' health be given in the evaluation of pesticides in their pesticidal use.

I certify that the above is a true and correct copy of the findings adopted by the Scientific Review Panel on November 28 2001.

/s/

John R. Froines, Ph.D
Chairman,
Scientific Review Panel