UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
OFFICE OF RESEARCH AND DEVELOPMENT
ENVIRONMENTAL CRITERIA AND ASSESSMENT OFFICE
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SUBJECT: Surrogate RfDs for Specific PAHs (Batavia Site/Batavia, New York)

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This memo is in response to a request from Justin LeBlanc of Alliance Technology for review of the proposal that oral RfDs for certain PAHs (acenaphthene, pyrene, naphthalene, anthracene) serve as surrogate RfDs for structurally similar PAHs (acenaphthene, benzo[g,h,i]perylene, 2-methylnaphthalene and phenanthrene, respectively).

As reviewed in the Drinking Water Criteria Document for Polycyclic Aromatic Hydrocarbons (U.S. EPA, 1990), data on noncarcinogenic effects for oral exposures to many PAHs are either nonexistent or provide insufficient information on which to base health effects criteria. Sufficient data for RfD derivation are available only for 6 PAHs: acenaphthene, anthracene, fluoranthene, fluorene, naphthalene and pyrene. Data are available from a 90-day gavage mouse study of a seventh PAH, acenaphthylene (cf. U.S. EPA, 1990), but the study is not suitable for derivation of an oral RfD, because the lowest dosage level in the study produced mortality. Critical effects and derived RfDs for these seven PAHs are listed in Table 1.

Table 1 shows that the effects of concern and the relative potencies to produce noncarcinogenic effects vary considerably among the seven PAHs for which data are available. This variation in toxicological behavior emphasizes the uncertainties associated with the necessary assumptions in deriving RfDs for PAH for which no data exist. It is uncertain if the RfD for any particular, suitably studied, PAH will protect against the possible, but unknown, systemic effects of another PAH.

Outlined below is a summary of the rationale as to why derivation of surrogate RfDs is not recommended:

1. Use of Acenaphthylene as a Surrogate for Acenaphthene

These two molecules differ only in that acenaphthylene has a double bond between carbons 1 and 2, while acenaphthene has a single bond between the same carbons. In a 90-day gavage administration, acenaphthylene doses as low as 100 mg/kg/day produced mortalities, but doses of acenaphthene as high as 175 mg/kg/day produced no apparent adverse effects.

2. Use of Pyrene as a surrogate for Benzo(g,h,i)perylene

As reviewed in the Drinking Water Criteria Document for Polycyclic Aromatic Hydrocarbons (U.S. EPA, 1990), there are no epidemiological or experimental data regarding the noncarcinogenic effects of oral exposure to benzo[g,h,i]perylene. Therefore, data is insufficient to evaluate whether use of the oral RfD for pyrene would provide adequate protection for exposure to benzo(g,h,i)perylene.

3. Use of Naphthalene as a Surrogate for 2-methylnaphthalene

As reviewed in the ATSDR Toxicological Profile on Naphthalene and 2-Methylnaphthalene (ATSDR, 1990), no information is available on the health effects of 2-methylnaphthalene in animals or humans following oral, dermal or inhalation exposure, and the only data that are available are acute intraperitoneal studies. Single intraperitoneal injections of either 2-methylnaphthalene or naphthalene (at similar dosage levels) caused similar necrotic effects in the lungs of mice (Buckpitt and Franklin, 1989), thus suggesting that health effects caused by the two compounds may be similar. However, intraperitoneal injections of 2-methylnaphthalene in rats are much less lethal than injections of naphthalene (Griffin et al., 1981). This difference in lethal potency may be related to the demonstrated differences in the metabolism of the two compounds. The metabolism of 2-methylnaphthalene proceeds via two divergent pathways, methyl group oxidation and epoxidation of the aromatic ring; naphthalene metabolism occurs via the aromatic ring epoxidation pathway only (Buckpitt and Franklin, 1989). Evidence is available that the methyl group oxidation pathway is the major metabolic fate of 2-methylnaphthalene in guinea pigs (Teshima et al., 1983) and rats (Melancon et al., 1982). The differences between the acute lethal potencies and metabolism of 2-methylnaphthalene and naphthalene appear sufficient to preclude the use of an oral RfD for naphthalene as an analogous RfD for 2-methylnaphthalene.

4. Use of Anthracene as a Surrogate for Phenanthrene

As reviewed in the Drinking Water Criteria Document for Polycyclic Aromatic Hydrocarbons (U.S. EPA, 1990), there are no epidemiological or experimental data regarding the noncarcinogenic effects of oral exposure to phenanthrene. Therefore, data is insufficient to evaluate whether use of the oral RfD for anthracene would provide adequate protection for exposure to phenanthrene.

In conclusion, it is our recommendation that oral RfDs for acenaphthylene, benzo[g,h,i]perylene, phenanthrene and 2-methylnaphthalene not be derived based on structural similarity only. Systemic toxicities need to be adequately tested in order to derive oral RfDs for these chemicals.

Please feel free to contact ECAO at FTS 684-7300 if we can be of further assistance.

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Table 1. Critical noncarcinogenic effects produced in animals in 13-week gavage exposure to PAHs.

PAH	Critical Effect	NOAEL (mg/kg/day)	LOAEL (mg/kg/day)	Chronic RfD (mg/kg/day)
acenaphthene	hepatic effects	175	350	6E-2[a]
acenaphthylene	mortality	NI[b]	100 (FEL)	ND[c]
anthracene	no effects observed	1000	NI[b]	3E-1[a]
fluoranthene	liver, kidney and hematologi-cal effects	125	250	4E-2[a]
fluorene	hematologi-cal effects	125	250	4E-2[a]
naphthalene	decreased body weight	50	100	4E-3[d]
pyrene	renal effects	75	125	3E-2[a]

[a] Source: U.S. EPA, 1990; 1991. Each of the principal studies used mice with the exception of the principal study for naphthalene which used rats.
[b] NI - Not identified.
[c] ND - Not determined.
[d] Currently under review by the RfD/RfC Work Group.

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