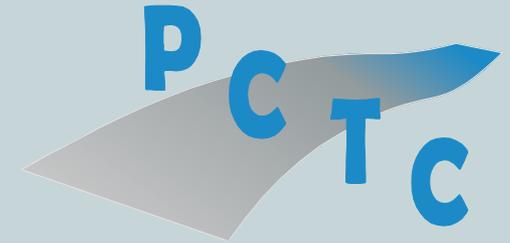


Rationale for Recommending an RPF Approach

Anne LeHuray

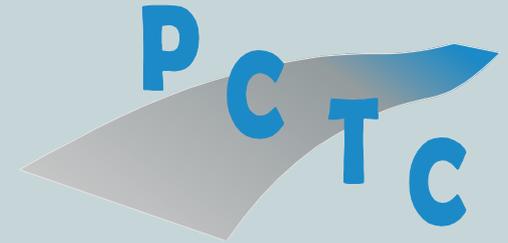
Pavement Coatings Technology Council

Introduction

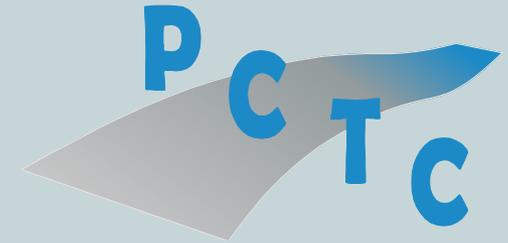


- Members of the Pavement Coatings Technology Council (PCTC) are the manufacturers of coatings and sealants used to protect and extend the life of paved surfaces and their suppliers
- For the SAB's consideration, a consortium of industry groups commissioned a detailed review of the Draft PAH RPF Approach document. Some of our comments are highlighted in this presentation, as well as in presentations that follow today.
- PCTC urges SAB members to review the written comments.

General Observations

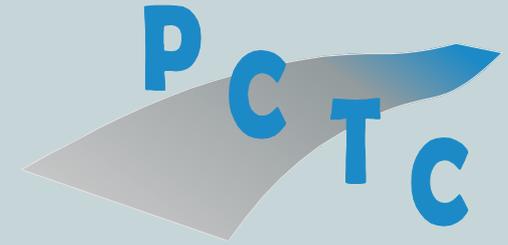


- According to the Draft PAH Potency Factor document "*The EPA RPF approach involves two key assumptions (1) a similar toxicological action of PAH components in the mixture and (2) interactions among PAH mixture components do not occur at low levels of exposure typically encountered in the environment*" (p. iv)."
- The Draft document does not provide sufficient scientific evidence or quantitative data to support the hypothesis of similar modes of action of the PAHs.
- **Similar concerns were expressed by NASA and DoD in comments submitted to EPA on October 28, 2009.**



Choice of B(a)P as the index compound

- The RPF approach relies on the 1994 B(a)P IRIS assessment and assumes the PAHs to be carcinogenic based on hypothesized toxicological similarities to B(a)P
 - EPA does not provide justification of toxicological similarity as needed per the EPA 2005 Cancer Guidelines
- The B(a)P IRIS assessment is currently being updated, with the final revised assessment scheduled for June 2011
- The current CSF of $7.3 \text{ (mg/kg/day)}^{-1}$ will undoubtedly give increased weight to more recent studies [Beland and Culp (1998) and Culp et al. (1998) data as summarized by Gaylor et al. (2000)], which suggest a CSF of $1.2 \text{ (mg/kg/day)}^{-1}$
- See Pages 3–4 of our submitted written comments for more detail.

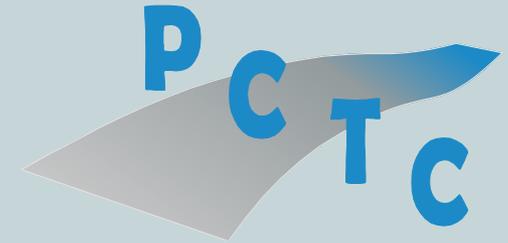


Criteria for the PAH RPF Approach

- Studies which contain pertinent PAH toxicology data regardless of whether the studied PAH was tested in conjunction with B(a)P should be evaluated.
- Example: Wood et al (1980) was excluded .
- EPA should examine how the choice of an index chemical influences the RPF values. The Wood et al (1980) data illustrates that the choice of index chemical can profoundly affect the resulting RFP.
- See Pages 4 –6 of our submitted written comments for more detail

Effect of Wood et al. (1980) Data on RPF Derivation

	EPA RPFs	Wood et al. (1980) Assuming Chrysene As Index Chemical
Benzo(a)pyrene	1	-
Chrysene	0.1	1
Benz[a]anthracene	0.2	0.4
Cyclopenta[c,d]pyrene	0.4	0.4



RPFs from Non-Cancer Endpoints

- RPFs from non-cancer endpoints should not be used when deriving RPF values.
- Example - dibenz[a,c]anthracene (DBaC_A)
 - DNA adduct, DNA damage, mutagenicity and cell transformation studies, are inappropriate for quantitative dose-response assessment.
 - An RPF = 4 for DBaC_A was based entirely on DNA adduct, DNA damage, mutagenicity and cell transformation studies.
 - At least four in vivo studies reported in the document show that DBaC_A is *not* tumorigenic in the mouse skin bioassay.
- See Page 17 of our submitted written comments for more detail.

Use of Studies with High Mortality

- The RPF approach states “unexplained mortality in treated or control animals” is a criterion for excluding studies from the RPF derivation. However, the following study was included in RPF derivation
- See Pages 21 -23 of our submitted written comments for more detail.

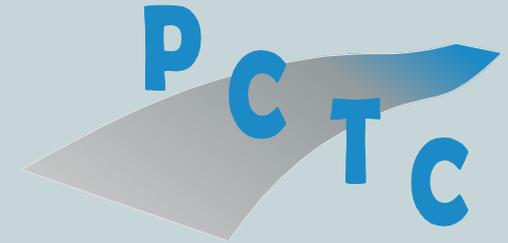
High Mortality Rates in Studies Used to Calculate RPFs

Reference	Exposure Route	PAH ¹	Dose Level	Initial Number of Animals	Mortality at Appearance of First Tumor (%)	Final Number of Animals	Mortality Overall (%)	Length of Experiment
Hoffmann and Wynder 1966	Dermal-CC	Control	0	20	NA	12	40%	15 months
	Dermal-CC	DBaeP	0.05	20	70%	0	100%	15 months
	Dermal-CC	DBaeP	0.05	20	30%	5	75%	15 months
	Dermal-CC	DBaeP	0.1	20	55%	4	80%	15 months
	Dermal-CC	DBahP	0.05	20	15%	0	100%	15 months
	Dermal-CC	DBahP	0.1	20	10%	0	100%	15 months
	Dermal-CC	DBaiP	0.05	20	5%	2	90%	15 months
	Dermal-CC	DBaiP	0.1	20	5%	2	90%	15 months
	Dermal-CC	DBaeF	0.05	20	10%	0	100%	15 months
	Dermal-CC	DBaeF	0.1	20	10%	0	100%	15 months

Notes:

Dermal-CC = dermal, complete carcinogenicity
 mg = milligram
 mg/kg = milligrams per kilogram
 NA = not applicable
 PAH = polycyclic aromatic hydrocarbon

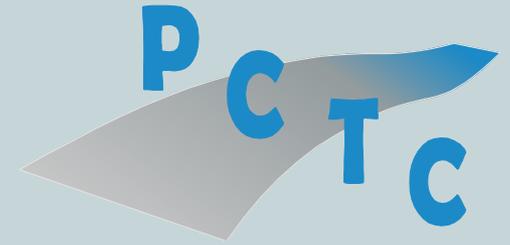
DBaeP = dibenzo[a,e]pyrene
 DBahP = dibenzo[a,h]pyrene
 DBaiP = dibenzo[a,i]pyrene
 DBaeF = dibenzo[a,e]fluoranthene



Purity and Identity of Chemical

- According to criteria in the Draft RPF Approach, studies in which the purity of the PAHs is “questionable,” should be excluded. However, RPF were derived from studies in which chemical identities were not confirmed
 - RPFs for benz[*l*]aceanthrylene and benz[*e*]aceanthrylene are derived from Nesnow et al. (1984)
 - RPFs for benz[*j*]aceanthrylene are derived from Mass et al. (1993)
 - RPFs for dibenzo[*a,l*]pyrene are derived from Cavalieri et al. (1991) and Nesnow et al. (1998). Cavalieri, et al. (1991)
- See Pages 25 -28 of our submitted written comments for more detail.

Summary



- Based on our review of the Draft PAH RPF Approach, detailed in our submitted written comments, the PCTC urges the SAB to consider whether the basis for this approach to development of PAH RPFs is scientifically sound at this time.

Thank you