TA-16 ORIGINAL

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Date: August 5, 2003
Refer to: ER2003-0501

Mr. David Cobrain
NMED-Hazardous Waste Bureau
2905 Rodeo Park Drive East
Building 1
Santa Fe, NM 87505-6303

SUBJECT: USE OF SURROGATE CHEMICALS IN RISK ASSESSMENTS

Dear Mr. Cobrain:

Attached is the discussion on the use of surrogate chemicals in the risk assessment process that you requested at the July 28, 2003 High Performance Team meeting for Solid Waste Management Unit (SWMU) 16-021(c)-99 (260 Outfall). The discussion includes an explanation of why surrogates are used in risk assessment, a list of chemicals and surrogates that we have used or may use in risk assessments, and supporting information for the use of the particular surrogates presented. As we discussed at the July 28th meeting, the utilization of surrogates is a common approach for assessing risk from chemicals that do have toxicity information available and is an alternative recommended by the U.S. Environmental Protection Agency in their Risk Assessment Guidance for Superfund, Volume 1, Human Health Evaluation (Part A).

It is our understanding that this is a programmatic issue and not solely related to the above referenced SWMU risk assessments. New Mexico Environment Department – Hazardous Waste Bureau's acceptance of the use of surrogates in general and the surrogates in the attachment in particular will be for all risk assessments conducted by the Laboratory's Risk Reduction and Environmental Stewardship - Remediation Services Project.

Please review the attached information and provide any questions, comments, and concerns to Richard Mirenda at (505) 665-6953.

Sincerely,

David McInroy, Acting Deputy Project Director
Remediation Services
Los Alamos National Laboratory

Sincerely,

David Gregory, Project Manager
Department of Energy
Los Alamos Site Operations

6429

DM/DG/RM/dv

Enclosure: Surrogate Chemicals in Risk Assessment Discussion (ER2001-0883)

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Surrogate Chemicals in Risk Assessment

One of the key pieces of information needed to assess the potential risk of a chemical or chemicals is the information on the toxicity to human receptors. EPA has developed databases on chemical toxicity to humans in the Integrated Risk Information System (IRIS) and the Health Effect Assessment Summary Tables (HEAST). The reference doses (RfDs) and cancer slopes factors (SFs) presented in these databases are the values used in calculating potential risk for each chemical and pathway being evaluated. However, some chemicals do not have toxicity information available in either IRIS or HEAST. In addition, EPA's National Center for Environmental Assessment (NCEA) does not have provisional toxicity values for some chemicals. The reasons for the lack of toxicity information is either because the chemical is not or has not been a concern and/or the available toxicity information has not been reviewed by EPA. In these cases, there are several options available and recommended in EPA's Risk Assessment Guidance for Superfund, Volume1 Human Health Evaluation Manual, Part A, Interim Final (EPA 540/1-89/002, 1989). These options include (1) address the potential risk in a qualitative manner, looking at magnitude of concentrations and frequency of detection, (2) calculating a value from available scientific literature using the EPA methodology, or (3) use a toxicity value for another chemical based on similar structure and assumed similar toxicity of the two chemicals. The assumption for the last alternative is that the known toxicity of one chemical is used to estimate the toxicity of another structurally related chemical for which data are lacking. In this fashion, a "surrogate" toxicity value is used to determine the potential risk from the chemical for which data are lacking.

The third alternative is often used because it allows the use of toxicity information that has been accepted by EPA and is more expeditious then trying to calculate a new toxicity value. In addition, a new calculated toxicity value has large uncertainties associated with it because of the acceptability of the literature data used to determine an RfD or SF for a chemical. The uncertainties surrounding the risk must be incorporated into the uncertainty discussion regardless of the approach used. In the case of a surrogate, the risk assessor must discuss whether the potential risk contributed by the chemical is an over- or underestimate. If it is concluded that it is potentially an underestimate, the risk assessor must decide whether the underestimate substantially affects the total risk, i.e., increases the potential risk by an order of magnitude or more. In most, if not all cases, to date, the chemicals detected that do not have toxicity data are infrequently detected and are reported at low concentrations (less than 1 mg/kg). Therefore, these chemicals have not been risk drivers and, if the risk is underestimated, do not affect the decision for a site.

Table 1 is a list of chemicals and surrogates that have either been used in past reports or may be used in future reports if the chemicals are detected. The information includes a brief description of the chemicals, the rationale for using the surrogate chemicals, and the structure of each chemical and surrogate. This list is not intended to be all-inclusive.

Table 1
Chemicals with Inadequate Toxicity Information and Corresponding Surrogate Chemicals

Chemical	Surrogate Chemical	Rationale
acenaphthylene	acenaphthene	structure similarity
2-amino-4,6-dinitrotoluene	2,6- dinitrotoluene	structure similarity
4-amino-2,6-dinitrotoluene	2,6- dinitrotoluene	structure similarity
benzo(g,h,i)perylene	pyrene	structure similarity
endosulfan I	endosulfan	Endosulfan I is an isomer of endosulfan
endosulfan II	endosulfan	Endosulfan II is an isomer of endosulfan
endosulfan sulfate	endosulfan	Endosulfan sulfate is the primary metabolite of endosulfan
endrin aldehyde	endrin	Endrin aldehyde is an impurity and breakdown product of endrin
endrin ketone	endrin	Endrin ketone is the primary metabolite of endrin
2-hexanone	2-butanone	structure similarity
isopropyltoluene	Isopropylbenzene	structure similarity
2-methylnaphthalene	naphthalene	structure similarity
3-nitroaniline	2-nitroaniline	structure similarity
4-nitroaniline	2-nitroaniline	structure similarity
2-nitrophenol	4-nitrophenol	structure similarity
phenanthrene	anthracene	structure similarity
phenanthrene	pyrene	structure similarity (Used by NMED)

acenaphthylene The surrogate chemical is acenaphthene. The difference between the two chemicals is a double bond located on the 5-carbon ring (Figure 1). The double bond strengthens the structure making acenaphthylene less reactive than acenaphthene.

2-amino-4,6-dinitrotoluene The surrogate chemical is 2,6-dinitrotoluene. The difference between the two chemicals is the addition of an amino group (NH_2), the position of that amino group and the position of the nitro group (NO_2) (Figure 2). Because there are fewer sites for reactions to occur on the surrogate 2,6-dinitrotoluene, the surrogate will be less reactive than 2-amino-4,6-dinitrotoluene.

4-amino-2,6-dinitrotoluene The surrogate chemical is 2,6-dinitrotoluene. The difference between the two chemicals is the addition of an amino group (NH_2) (Figure 2). Because there are fewer sites for reactions to occur on the surrogate 2,6-dinitrotoluene, the surrogate will be less reactive than 4-amino-2,6-dinitrotoluene.

benzo(g,h,i)perylene The surrogate chemical is pyrene. The difference between the two chemicals is the addition two benzene rings (Figure 3). The additional benzene rings add stability to the structure making the surrogate pyrene more reactive than benzo(g,h,i)perylene.

endosulfan I The surrogate chemical is endosulfan. Endosulfan I is an isomer of endosulfan. These chemicals have the same chemical weight and the same molecules. The melting point of

endosulfan and endosulfan I is 106°C and 108°C, respectively. A comparison of structure is presented in Figure 4.

endosulfan II The surrogate chemical is endosulfan. Endosulfan II is an isomer of endosulfan. These chemicals have the same chemical weight and the same molecules. The melting point of endosulfan and endosulfan II is 106°C and 207°C, respectively. A comparison of structure is presented in Figure 4.

endosulfan sulfate The surrogate chemical is endosulfan. Endosulfan is converted to endosulfan sulfate and endosulfan diol in laboratory animals. Endosulfan and its primary metabolite, endosulfan sulfate, exhibit similar toxicities and are both believed to be responsible for the toxicity observed in animals. The dose that kills 50% of treated laboratory animals (LD50) for endosulfan is listed in the Merck Index as 43 mg/kg for male rats and 18 mg/kg for female rats; endosulfan sulfate was not listed. The Registry of Toxic Effects of Chemical Substances (RTECS) lists only one citation for endosulfan sulfate, which is titled "Analytical Reference Standards and Supplemental Data: The Pesticides and Industrial Chemicals Repository" (USDHHS 1987, 70943). This source listed the LD50 value of endosulfan sulfate as 18 mg/kg for rats. While there were no specifics given on the gender of the rats, this LD50 supports the statement that endosulfan sulfate is toxicologically similar to endosulfan (ATSDR 1997, 56531.3). The use of endosulfan as a surrogate for endosulfan sulfate could lead to an overestimation of the risk posed by endosulfan sulfate because the other primary metabolite (endosulfan diol) could be mainly responsible for the toxicity instead of endosulfan sulfate. The use of endosulfan as a surrogate for endosulfan sulfate is not likely to lead to an underestimate of the risk because the two chemicals exhibit similar toxicities (LD50s) observed in animals. A comparison of structures is presented in Figure 5.

endrin aldehyde The surrogate chemical is endrin. Endrin aldehyde is an impurity and breakdown product of Endrin. Photochemical isomerization of endrin was observed after exposure of thin layers of solid endrin on glass to sunlight (ATSDR 1997, 56531.3). Minor amounts of endrin aldehyde were formed in this reaction. Endrin is also sensitive to transformation by heat, yielding primarily the pentacyclic ketone and endrin aldehyde at temperatures greater than 230°C (ATSDR 1997, 56531.3). A comparison of structures is presented in Figure 6.

endrin ketone The surrogate chemical is endrin. Endrin ketone is a breakdown product of endrin. Photochemical isomerization of endrin, primarily to the pentacyclic ketone commonly called endrin ketone, was observed after exposure of thin layers of solid endrin on glass to sunlight (ATSDR 1997, 56531.3). Results of seasonal studies indicated that this isomerization proceeds with a half-life of 5 to 9 days in intense summer sunlight, with complete conversion to endrin ketone in 15 to 19 days. A comparison of structures is presented in Figure 6.

2-hexanone The surrogate chemical is 2-butanone. The difference between the two chemicals is that 2-hexanone has a longer chain with two carbon and four hydrogen atoms. Under the same conditions, these chemicals react similarly. 2-hexanone will be less stable due to the elongated shape causing a polarity difference between the oxygen and the carbon in the number six position (Figure 7).

4-isopropyltoluene The surrogate chemical is isopropylbenzene based on structural similarity. The difference between the two chemicals is a carbon molecule in the number two position for 2-isopropyltoluene (Figure 8). Isopropyltoluene is more reactive because the additional carbon affords an additional reaction site.

2-methylnaphthalene The surrogate is naphthalene based on structural similarity. The difference between the two chemicals is a carbon molecule in the number three position for 2-methylnaphthalene (Figure 9). 2-methylnaphthalene is more reactive because the additional carbon affords an additional reaction site.

3-nitroaniline The surrogate chemical is 2-nitroaniline based on structural similarity. The difference between the two chemicals is the position of the nitro group (NO_2) (Figure 10). Under the same conditions, these chemicals react similarly.

4-nitroaniline The surrogate chemical is 2-nitroaniline based on structural similarity. The difference between the two chemicals is the position of the nitro group (NO_2) (Figure 10). Under the same conditions, these chemicals react similarly.

2-nitrophenol The surrogate chemical is 4-nitrophenol based on structural similarity. The difference between the two chemicals is the position of the nitro group (NO_2) (Figure 11). Under the same conditions these chemicals react similarly.

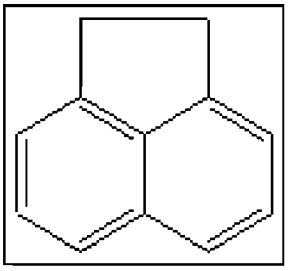
phenanthrene The surrogate chemical is anthracene based on structural similarity. The difference between the two chemicals is the position of the benzene rings (Figure 12). Under the same conditions, these chemicals react similarly. Phenanthrene is more polar and therefore more reactive than anthracene. NMED uses pyrene as a surrogate (Figure 13).

References

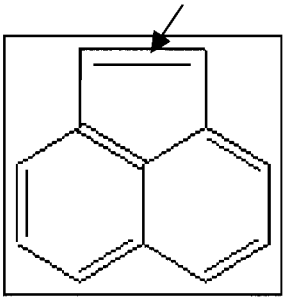
ATSDR (Agency of Toxic Substances and Disease Registry) 1997. "Toxicological Profiles on CD-ROM; Toxicological Profiles of Endosulfan, Endrin, and Endrin Aldehyde" (ATSDR 1997, 56531.3)

EPA (US Environmental Protection Agency), December 1989. "Risk Assessment Guidance for Superfund (RAGS), Volume I, Human Health Evaluation Manual (Part A), Interim Final," EPA 540/1-89/002, OSWER 9285.7-01A, Office of Emergency and Remedial Response, Washington, D.C. (EPA 1989, 08021)

USDHHS (US Department of Health and Human Services) April 1987. "Registry of Toxic Effects of Chemical Substances," 1985-86 Edition, Volume 3, Doris V. Sweet, ed., US Government Printing Office, Washington, D.C., 1988. (USDHHS 1987, 70943)



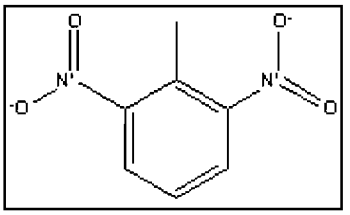
Acenaphthene
(Surrogate)



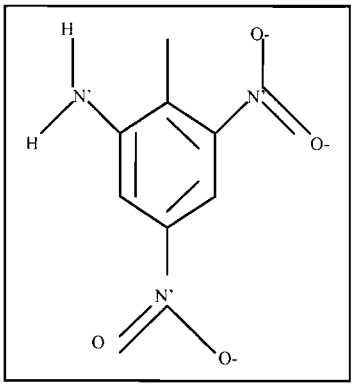
Acenaphthylene

Comment: The difference between the two chemicals, a double bond located on the 5-carbon ring, is indicated by an arrow.

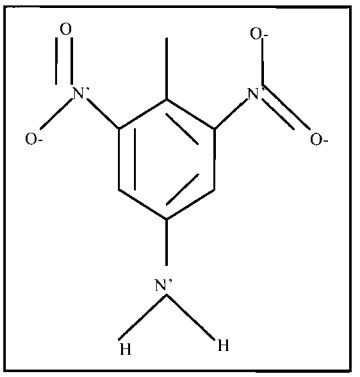
Figure 1. Structure comparison between acenaphthene and acenaphthylene



2,6-DNT
(Surrogate)

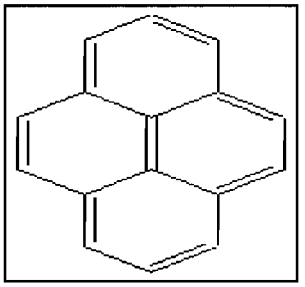


2-Amino-4,6-DNT

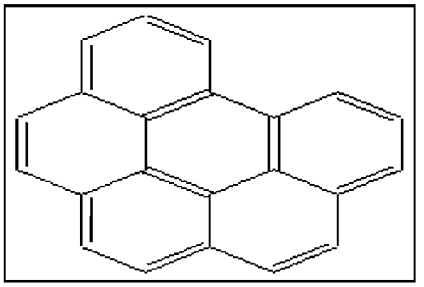


4-Amino-2,6-DNT

Figure 2. **Structure comparison among 2,6-DNT, 2-amino-4,6-DNT, and 4-amino-2,6-DNT**



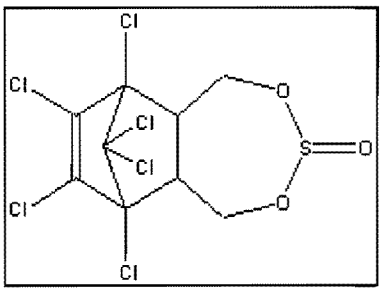
Pyrene
(Surrogate)



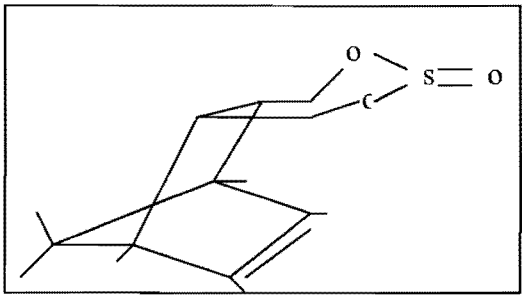
Benzo(g,h,i)perylene

Comment: The difference between the two chemicals, two additional benzene rings, is indicated by an arrow.

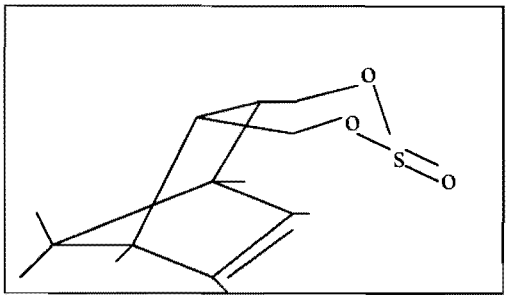
Figure 3. Structure comparison between pyrene and benzo(g,h,i)perylene



Endosulfan
(Surrogate)

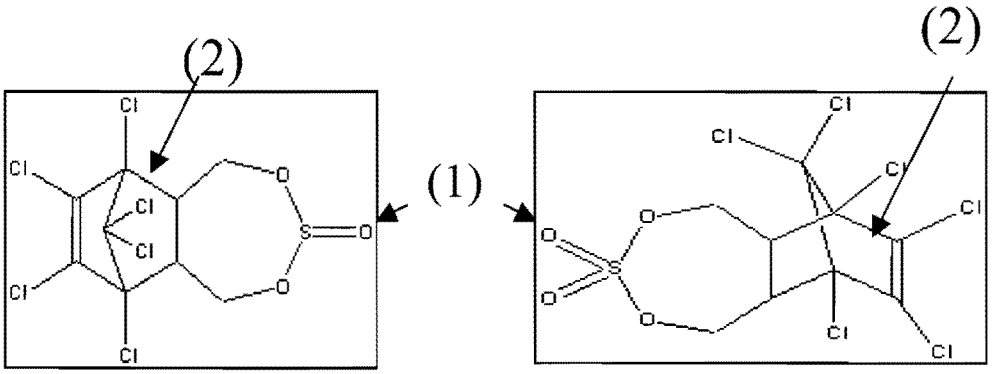


Endosulfan I



Endosulfan II

Figure 4. **Structure comparison among endosulfan and isomers endosulfan I and endosulfan II**

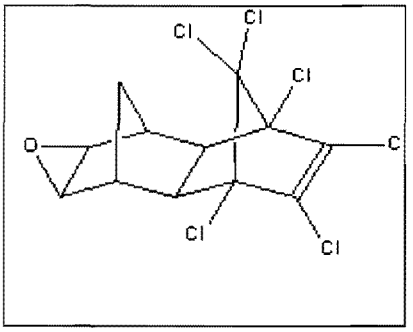


Endosulfan (Surrogate)

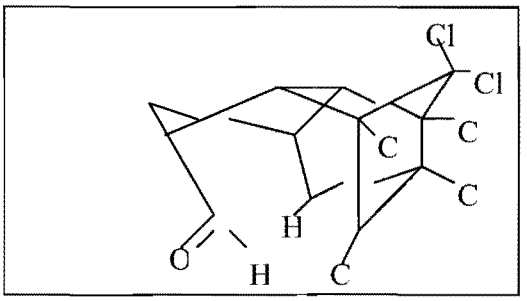
Endosulfan Sulfate

Comment: The differences between the two chemicals, (1) the number of oxygen molecules off the sulfate on the eight-sided ring, and (2) the shape of the six-sided ring, is indicated by arrows.

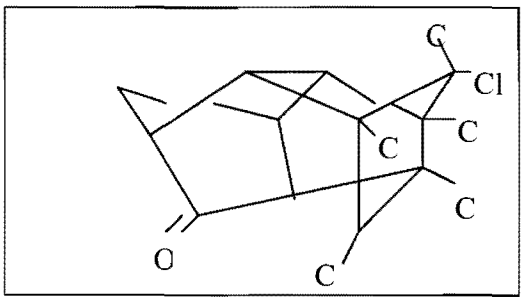
Figure 5. Structure comparison between endosulfan and endosulfan sulfate



Endrin
(Surrogate)

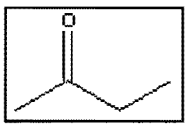


Endrin Aldehyde

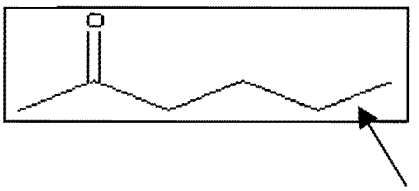


Endrin Ketone

Figure 6. **Structure comparison among endrin, endrin aldehyde, and endrin ketone**



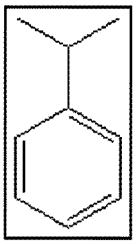
2-Butanone
(Surrogate)



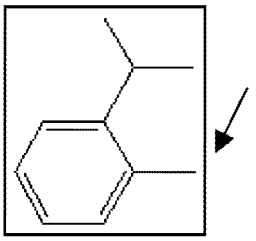
2-Hexanone

Comment: The difference between the two chemicals, two carbon and four hydrogen atoms, is indicated by an arrow.

Figure 7. Structure comparison between 2-butanone and 2-hexanone



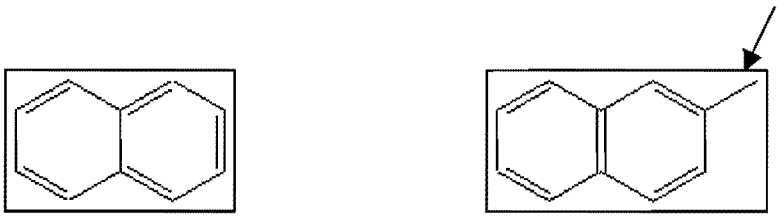
Isopropylbenzene
(Surrogate)



4-Isopropyltoluene

Comment: The difference between the two chemicals, a carbon molecule and two hydrogen molecules in the number two position, is indicated with an arrow.

Figure 8. Structure comparison between isopropylbenzene and 4-isopropyltoluene

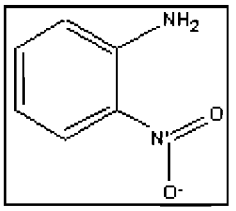


Naphthalene (Surrogate)

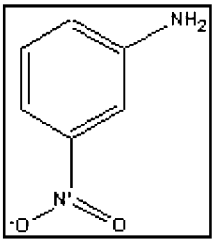
2-Methylnaphthalene

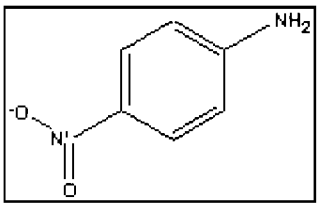
Comment: The difference between the two chemicals, a carbon molecule and two hydrogen molecules in the number three position, is indicated by an arrow.

Figure 9. Structure comparison between naphthalene and 2-methylnaphthalene



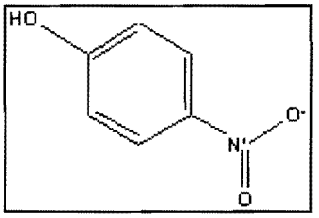
2-Nitroaniline
(surrogate)

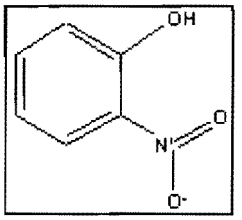




3-Nitroaniline 4- Nitroaniline

Figure 10. Structure comparison among 2-nitroaniline, 3-nitroaniline, and 4-nitroaniline

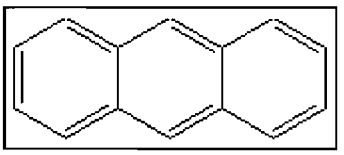


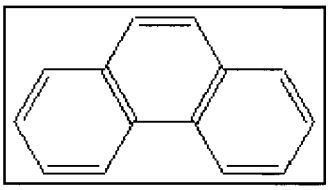


4-Nitrophenol (Surrogate)

2-Nitrophenol

Figure 11. Structure comparison between 4-nitrophenol and 2-nitrophenol

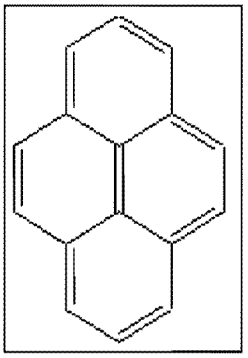


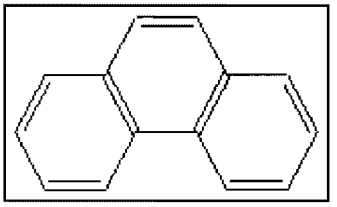


Anthracene (Surrogate)

Phenanthrene

Figure 12. Structure comparison between anthracene and phenanthrene





Pyrene (Surrogate)

Phenanthrene

Figure 13. Structure comparison between pyrene and phenanthrene