ASPHALT CATEGORY ANALYSIS AND HAZARD CHARACTERIZATION

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EXECUTIVE SUMMARY

The Asphalt Category in the HPV Challenge Program is aligned with the European Union's substances category "Bitumen (Asphalt) and Vacuum Residues". The asphalt category comprises a single group of heavy residual streams derived from the high temperature vacuum distillation of petroleum. These complex substances typically boil above 450^{0}C (842^{0}F) [range of 400-550^{0}C (752-1021^{0}F)], have high molecular weights (500 - 5000), and high viscosity (300-500 cSt @ 100-135°C) in order to meet the use specifications in commercial asphalt formulations. Two category members, asphalt [CAS# 8052-42-4] and oxidized asphalt [CAS # 64742-93-4] represent >99% of all asphalt material end-uses such as asphalt paving (84%) and asphalt roofing (15%) applications. Less than 1% is used for other purposes such as waterproofing, damp proofing, insulation and paints (AI, 1990a)

The uses of asphalt create a dichotomous hazard profile between the ambient-temperature substances and the fumes generated from heated products. Toxicity and environmental fate of the ambient-temperature substances are defined by the refining step of vacuum distillation. Evaluation of their common physical-chemical properties is sufficient to satisfy HPV requirements for all substances in this category since exposures of both humans and the environment are predominantly to vapors from asphalt rather than to the asphalt itself. Toxicity and environmental fate of the fumes generated from heated in-use products are directly related to the temperature of fume generation. Increasing temperatures dramatically increases the fume quantity and also changes the physical-chemical properties of the fume. High temperature generation can also increase the PAH content of the fume. A "real world" sample that mimics fume observed in realistic high temperature field asphalt application (e.g., roofing) has been used to "bound" the composition of the fume from all members of the asphalt category for human health effects testing.

Physical-chemical properties, environmental fate, environmental effects and human health effects are summarized below and discussed in the body of the category analysis. The mammalian health data are derived primarily from inhalation studies utilizing asphalt fume or fume condensate as the test materials.

Physical-Chemical Properties:

The physical-chemical characteristics of the members of the Asphalt Category show that these substances are solid to semi-solid viscoelastic substances with extremely high boiling temperatures (>450 °C). They have negligible vapor pressure, partition coefficients estimated to be typically >10, and are essentially insoluble in water.

Environmental Fate:

At ambient temperatures the semi-solid to solid nature of substances in the Asphalt Category and negligible vapor pressure and water solubility limit their distribution to different environmental compartments. Asphalts will tend to remain within the terrestrial or aquatic compartment to which they were released. During the applications of asphalts, fumes may be generated when the material is heated, and these fumes may condense onto local surfaces as they cool. Any vapors that remain suspended have the potential to interact with tropospheric OH radicals, and in this manner indirectly photodegrade within a matter of hours to a few days. Although hydrocarbons can be utilized as an energy source by microorganisms, asphalts would not dissolve or disperse in

a manner to augment microbial attack. Due to the bulk properties of asphalt, a release to the environment would not result in measureable biodegradation.

Ecotoxicity:

The constituent hydrocarbons making up asphalt and vacuum residue are of such high molecular weight and low solubility that such materials would not be expected to cause acute or chronic toxicity in aquatic organisms. Data from petroleum streams with hydrocarbon structures similar to asphalts (e.g., lubricating base oils and aromatic extracts of vacuum distillates produced during manufacture of lubricant base oils) elicited no acute or chronic aquatic toxicity when tested as water accommodated fractions up to a loading rate of 1000 mg/L. Asphalts also would not be expected to cause acute or chronic toxicity in aquatic organisms.

Human Health Effects:

Inhalation of asphalt fume is considered the route of exposure most relevant to hazard assessment for humans both in the workplace and the general population. LOAEL and NOAEL designations for repeated dose and developmental/ reproduction studies for read-across to untested category members are derived from inhalation study results.

Acute Toxicity: Asphalts and asphalt fumes demonstrate low acute toxicity by oral (LD50 rats>5.0g/kg), dermal (LD50 rabbits>2.0g/kg) and inhalation (LC50>>94.4mg/m^3) routes of exposure. Asphalts cause slight dermal irritation and mild to moderate eye irritation and are not skin sensitizers. Effects in humans under field construction conditions include mild and transitory eye irritation, nasal and throat irritation with exposure to fumes. Some skin irritation has been reported with exposure to heated asphalt or co-exposures to asphalts with diesel fuel, coal tar or fiberglass.

Repeated Dose Toxicity: Nose-only inhalation exposure of rats to roofing or paving asphalt fume condensate over durations of 28 (OECD 422) to 90 days respectively resulted in a similar range of LOAEL and NOAEL values. Overall effects were decreased body weight gain and food consumption. Effects on the respiratory system included increased lung weights and slight to moderate histopathologic changes in nasal cavities and lungs at the highest exposure levels. In general asphalt and asphalt fume condensates do not induce severe toxicity at tested doses. The read-across values for untested category members are:

LOAEL = 149 to 297 mg/m^3 [highest doses tested in each study]
NOAEL = 28 to 30 mg/m^3

In Vitro Genetic Toxicity – Gene mutation: Whole asphalts are non-mutagenic or weakly mutagenic with metabolic activation. Positive results in bacteria and slight activity in mammalian cells with metabolic activation have been induced by some asphalt fume condensates. Severity of effect correlated with the temperature under which fumes were generated.

In Viivo Genetic Toxicity – Cytogenetics: Vacuum residuum administered orally or asphalt fume condensate administered by inhalation to laboratory animals under realistic fume generation and exposure conditions did not induce cytogenetic damage [chromosomal or micronucleus]. DNA adducts and strand breaks have been reported in some systems in the absence of definitive

cytogenetic damage. Human data are highly variable and confounded by co-exposure to coal tar or other biologically active materials. Overall asphalts and asphalt fumes are not clastogenic.

Reproductive and Developmental Toxicity: Assessment of reproductive toxicity was derived from the reproductive portion of OECD 422 Combined Repeated Dose Toxicity Study with Reproductive/ Developmental Toxicity Screening Test. Exposure to oxidized roofing asphalt fume condensate does not induce adverse effects on reproductive organs or on reproductive or developmental parameters, demonstrating that asphalt fume condensate is not a reproductive toxicant. The read-across value for reproductive toxicity for untested substances in this category is NOAEL = 293.7 mg/m^3, the highest concentration tested.

Carcinogenicity: Two year exposure of rats by nose-only inhalation up to 172.5 mg/m^3 to a partially oxidized bitumen fume condensate from the headspace of hot storage tank containing semi-blown paving bitumen (50/70 pen) representative of workplace exposure did not result in excess tumors in any organ system.

This testing program demonstrates that asphalt and asphalt fumes have generally low toxicity profiles for human health endpoints. Environmental results show asphalts are insoluble, not biodegradable and would not be expected to cause acute or chronic toxicity in aquatic organisms.

1. DESCRIPTION OF ASPHALT CATEGORY

The Asphalt Category for the HPV Challenge Program is aligned with the European Union's substances category "Bitumen (Asphalt) and Vacuum Residues". This allows harmonized efforts to collect and interpret data and potentially to harmonize risk assessments and risk management practices on petroleum products worldwide. Asphaltic materials such as asphalt, oxidized asphalt, vacuum residuum, hydrodesulfurized vacuum residuum, decarbonized residuum and petroleum resins are all residual streams derived from the vacuum distillation of petroleum. Most of these streams are either sold as is, blended together, or subsequently processed (air blowing or solvent deasphalting) to produce a variety of end use asphalt products that achieve specific product performance specifications. Two category members, asphalt [CAS #8052-42-4] and oxidized asphalt [CAS #64742-93-4] represent >99% of all asphalt material used in the USA and Europe (road-paving asphalt [84%] and roofing asphalt [15%] applications). Petroleum resins are low volume materials that end up in asphalt formulations or in specialty product use applications such as pipe coatings, roofing adhesives, paints, lubricants, etc. (AI, 1990a).

The six members of this HPV category, listed in Appendix A, all have high carbon to hydrogen ratios with carbon numbers predominantly greater than C25, boiling point ranges >400^{0}C, high viscosity and negligible vapor pressure (Table 1).

Table 1: Typical Physical/Chemical Properties of Asphalt Category Members

CAS Number	Hydrocarbon Chain Length	Boiling Point	Softening Point	Vapor Pressure	Specific Gravity	Reference
Asphalt (Penetration) 8052-42-4	> C25	>470^{0}C	30-60^{0}C	Negligible	0.95-1.1	[1-4]
Asphalt (Hard) 8052-42-4	> C25	>550^{0}C	60-75^{0}C	Negligible	NA	[1, 2]
Vacuum Residues 64741-56-6	> C34	>495^{0}C	NA	Negligible	0.98-1.1	[1]
Raffinates, Residual oil Decarbonization 64742-07-0	> C34	>495^{0}C	NA	Negligible	NA	[1]
Petroleum Resins 64742-16-1	NA	>482^{0}C	NA	Negligible	0.94	[1, 5]
Residues, Hydro-desulfurized vacuum 64742-85-4	> C34	>495^{0}C	NA	Negligible	NA	[1]
Asphalt, Oxidized 64742-93-4	>C25	>400^{0}C	60-130^{0}C	Negligible	1.0-1.1	[1-4]

NA = Data not available
1 - US EPA, TSCA Chemical Inventory, 2003.
2 - CONCAWE, 1992.
3 - CONCAWE, 2001.
4- Marathon Ashland Petroleum Asphalt and Oxidized Asphalt MSDS sheet, 1998;
5- Pennzoil 2600 Vis Resin MSDS sheet, 1998

1.1 Asphalt Production

In the United States, approximately 33 million tons of asphalt materials were produced in 2000 (AI, 2001). Modifying the refining processes can create different types of asphalts, ranging from sticky liquids to heavy brittle solids with variable physical-chemical properties.

Each step in the refining process, beginning with the residuum from atmospheric distillation, is designed to extract the maximum high value distillates from the residue until only the high boiling, high molecular weight components remain to be thermocracked, marketed as commercial asphalt, or as blending components of asphalts or fuel oils. With heavy crude oils, the vacuum residuum can often be "commercial asphalt". With lighter crude oils, these residues are feedstock for further processing. The steps in asphalt production are fully described in Appendix B. The asphalt category does not include asphalts mixed with industrial process oils or heavy distillates (fluxed asphalts), or asphalts to which have been added emulsifiers or elastomers which alter the chemical composition of the finished product.

These streams and variations of them are typically used to produce the three main types of commercial asphalts (CONCAWE, 1992).

1. Penetration Grade (PG - asphalt cements, viscosity-grade asphalts) is produced from crude oil atmospheric distillation residues by further processing such as vacuum distillation (straight run asphalts), thermal conversion, partial oxidation (air rectification/semi-blowing) or solvent precipitation. A combination of these processes can be used to meet application specifications for road surfacing or in roofing applications.

2. Hard Asphalts (Hard Bitumens) are manufactured using processes similar to penetration grades but have lower penetration values and higher softening points. They are hard and more brittle, and are used primarily in the manufacture of asphalt paints and enamels.

3. Oxidized (Air blown) Asphalts are produced by passing air through hot, soft asphalt feedstock under controlled conditions, producing a higher softening point material with reduced susceptibility to changes in temperature and greater resistance to imposed stress. Applications include roofing materials, waterproof papers, electrical components, pipe coating, undersealing of concrete pavements, hydraulic applications, membrane envelopes, and the manufacture of paint.

Commercial uses and descriptive terms for asphalt products are found in Appendix C.

Asphalts are not coal tar. Asphalts have been confused with coal tar and coal tar pitch, which can also be used for roofing and paving applications because both materials have a "tarry" consistency (Puzinauskas and Corbett, 1978). Outside of the US (e.g. Europe), coal tar and coal tar pitch was used in road building before and during World War II due to a shortage of asphalt cement. However, coal tar materials have apparently not been used in asphalt paving formulations after the 1970s (Kriech, et. al, 1997; Blackburn, et al, 1999). Coal tar and coal tar pitch are obtained as a byproduct of the destructive distillation of bituminous coal to produce coke by thermal cracking at high temperatures (458-1214^{0}C; 850-2200^{0}F). Coal tar contains relatively high levels of condensed-ring aromatic compounds with a greater proportion of unsubstituted polycyclic aromatic compounds (PAC) in the toxicologically active 3-7 ring size range. In contrast, asphalts contain much larger proportions of high molecular weight paraffinic and naphthenic hydrocarbons and their derivatives that, because of their size, viscosity, and limited solubility are not readily bioavailable

and have minimal toxicological activity. Thus, measurements of routinely monitored polycyclic aromatic hydrocarbons (PAH) such as benzo(a)pyrene, as is commonly done for coal-derived product, are not useful indicators of potential carcinogenic activity of asphalts because the carcinogenic PAH are present in extremely low concentrations and most asphalt PAC are alkylated. Fumes generated from asphalt are primarily aliphatic with a high proportion of saturates (60%, Brandt et al., 1985) and demonstrate much less toxicological activity than coal tar fumes which are comprised almost entirely of aromatic compounds (>99%). Study results presented in this test plan do not include data for coal tar or asphalt containing coal tar.

1.2 Composition of Asphalts

The chemistry of asphalt products is very complex because of the complex nature of the petroleum crude oils from which they are derived. The chemistry is also affected by the varying refining processes designed to meet specifications of performance rather than of a set chemical composition. Asphalts are comprised of asphaltenes, resins, aromatic and saturated components. Asphalts are regarded as colloidal systems consisting of micelles dispersed in an oily matrix of components with lower molecular weight (Witherspoon, 1962; IARC, 1985; Groenzin and Mullins, 1999, 2000). The micelles are considered to be asphaltenes with an adsorbed sheath of aromatic resins of high molecular weight as a stabilizing solvating layer. Moving away from the center of the micelle, there is a gradual transition to less aromatic resins, and the layer extends outward into the less aromatic oily dispersion residuum.

The major chemical groups in produced asphalt are described as follows:

Asphaltenes: brittle brown-black amorphous solids, which are highly condensed aromatic compounds with molecular weight 2000-5000, constitute 5-25% of the weight of asphalts. They are comprised of one or two chromophores containing 4 to 10 fused rings each, with a significant number of alkyl substituents. A higher proportion of asphaltenes are present in the harder asphalts.

Resins: brown-black, adhesive, shiny solids or semi-solids. Comprised of heterogeneous polar aromatic compounds with small amounts of oxygen, nitrogen, and sulfur with molecular weights of 800-2000, constitutes 15-25% of the weight of asphalts. Resins can be considered lower molecular weight asphaltenes and are dispersing agents for asphaltenes. The proportion of resin to asphaltenes governs to a degree the solidity or gel-type characteristic of the asphalt

Aromatic oil components: viscous dark brown liquids containing mainly carbon, hydrogen and sulfur with minor amounts of oxygen and nitrogen, with a molecular weight of 500-900, constitute 45-60% of the weight of the asphalt. They are compounds with aromatic and naphthenic-aromatic nuclei with side chain constituents.

Saturated oil components: viscous liquids or solids ranging from straw to water-white color, consisting mainly of long chain saturated hydrocarbons with some branched chain compounds, alkyl aromatics with long side chains and cyclic paraffins (naphthenes), with a molecular wt of 500-1000, constitute 5-20% of the weight of the asphalt.

The proportions of the chemical groups vary in asphalts because of significant differences in petroleum crude oils that vary from field to field and even from different locations within the same field, as well as differences in refining processes.

Elemental analyses indicate that most asphalts contain 79-88 weight % (wt %) carbon, 7-13 wt% hydrogen, traces to 8 wt% sulfur, 2-8 wt% oxygen, and traces to 3 wt% nitrogen (Speight, 1992) and trace amounts of vanadium, nickel, aluminum and silicon. The variability of components is primarily a reflection of the source of the crude oil (Magaw et al., 2000; Table 2).

Table 2: Elemental analysis of asphalts from different crude petroleum sources

Crude Source	Carbon wt %	Hydrogen wt %	Nitrogen wt %	Sulfur Wt %	Oxygen wt %	Vanadium Ppm	Nickel ppm
Mexican blend	83.77	9.91	0.28	5.25	0.77	180	22
Arkansas- Louisiana	85.78	10.19	0.26	3.41	0.36	7	0.4
Boscan	82.98	10.45	0.78	5.43	0.29	1380	109
California	86.77	10.94	1.10	0.99	0.20	4	6
Lloydminster 150/200	83.9	10.0	0.5	5.5	0.6	174	86
Lloydminster 200/300	84.1	10.59	0.5	6	NA	138	77
Wyoming Sour	82.3	10.6	0.54	4.7	0.8	220	56
Wyoming Sour	85.7	10.59	0.54	5.4	NA	163	36
Redwater AC-8	86.5	11.3	0.66	1.9	0.9	146	63
Redwater AC-5	86.6	10.6	0.9	1.9	1.0	100	55
California AR-4000	81.6	10.8	0.77	6.9	0.9	310	145
Coastal AR-2000	81.9	10.3	0.9	8.3	NA	266	135
CA Valley AR-4000	85.6	10.5	1.10	1.3	1.1	37	95
CA Valley AR-2000	87.0	10.5	1.15	2.9	NA	33	11
Boscan AC-30	83.7	10.2	0.70	6.4	0.8	1480	142
Boscan AC-10	83.2	10.3	0.70	6.9	NA	1165	117

SHRP, 1993; NIOSH, 2000; Speight, 1992

Crude oil is processed to make asphalt via atmospheric distillation followed by vacuum distillation (See Figure B-1). In step two of this process, the atmospheric residues are further processed under lower pressures and temperatures below those that cause significant thermal cracking (or pyrolysis). This results in the 3-7 ring polycyclic aromatic hydrocarbon (PAH) content in asphalt to be in the low parts per million range (AI, 1990a). The manufacturing and recommended use temperatures of asphalt do not facilitate formation of 3-7 ring PAHs.

Although the total sulfur content of asphalts may vary considerably (trace to 8 wt %), the sulfur does not influence toxicity from exposure to asphalt or asphalt fume because the sulfur is in the form of heterocyclic sulfur compounds with multiple fused rings and large molecular weights due to alkylation, resulting in minimal bioavailability. Some sulfur is released as H_2S and low molecular weight mercaptans but these compounds are present in very low concentrations in freshly generated asphalt fumes (Gamble et al., 1999; Fraunhofer, 2003)

1.2.1 Asphalt fumes

Asphalt fume is a visible airborne condensation product of lower boiling volatile components of petroleum asphalt that may be inhaled or deposited on skin and clothing. When asphalts are heated to facilitate paving or roofing applications, the lighter, more volatile components are distilled into the atmosphere. As these components cool, they condense forming small droplets of liquid (fume), some of which have an effective diameter of less than 12.5 microns and are considered respirable (AI, 1990b; Brandt et al., 1985). The temperature of fume generation affects both the relative proportions of individual PAHs in the fume and the amount of fume generated. The temperature-induced variations in fume composition and amount of fume generated have significant toxicological implications as described below. It has been reported that 80-fold more fume is given off at 250^0C (482^0F) than at 160^0C (320^0F), hence appropriate temperature control can considerably reduce emissions from asphalts (CONCAWE, 1992).

Asphalt products are required to be heated to maintain fluidity during bulk transportation and storage. This work practice can result in the generation of toxicologically significant concentrations of H_2S in the vapor spaces of storage tanks and bulk transport compartments. While creating a potential for acute overexposure to H_2S during gauging and unloading operations, the relative concentration of H_2S in relation to total particulate matter, benzene soluble matter or polycyclic aromatic hydrocarbons, in freshly generated asphalt fume is insignificant (Gamble et al, 1999; Fraunhofer, 2003).

2. CATEGORY DEFINITION AND JUSTIFICATION

The Asphalt Category in the HPV Challenge Program is aligned with the European Union's substances category "Bitumen (Asphalt) and Vacuum Residues". The Asphalt Category comprises a single group of heavy residual streams derived from the high temperature vacuum distillation of petroleum. These complex substances typically boil above 450^0C (842^0F) [range of 400-550^0C (752-1021^0F)], have high molecular weights (500 - 2000), and high viscosity (300-500 cSt @ 100-135°C) in order to meet the use specifications in commercial asphalt formulations. Two category members, asphalt and oxidized asphalt represent >99% of all asphalt material end-uses such as asphalt paving (84%) and asphalt roofing (15%) applications. Less than 1% is used for other purposes such as waterproofing, damp proofing, insulation and paints (AI, 1990a)

The uses of asphalt create a dichotomous hazard profile between the ambient-temperature substances and the fumes generated from heated products. The Testing Group believes the toxicity and environmental fate of the ambient-temperature substances are defined by the refining step of vacuum distillation. Subsequent processing (solvent extraction, air blowing, etc) to achieve product specifications does not alter the hazardous properties. Evaluation of their common physical-chemical properties is sufficient to satisfy HPV requirements for all substances in this category.

The Testing Group also believes the toxicity and environmental fate of the fumes generated from heated in-use products is directly related to the temperature of fume generation. Increasing temperature dramatically increases the quantity and also changes the physical-chemical properties of the fume. High temperature can also increase the PAH content of the fume. A sample that mimics fume observed in hot asphalt application (e.g., roofing) is appropriate to "bound" the composition of the fume from all members of the asphalt category.

3. TEST MATERIALS FOR MAMMALIAN ENDPOINTS

3.1 Previous Studies

Asphalt fumes generated under a range of heating conditions have been tested by inhalation, by dermal application as a fume condensate, and *in vitro*. Generating conditions significantly affected the composition and reliability of the test materials and subsequent toxicological results. Asphalt fumes generated experimentally at high temperature are more likely to contain carcinogenic PAC than fumes generated at the lower temperatures usually seen in field samples (McCarthy et al, 1999; NIOSH, 2000). Fume generation intervals have been reported to range from 4-16.5+ hours (Niemeier et al., 1988) or approximately 6 hours (AI, 1990a) to produce sufficient fume for testing. Asphalt heated to 600^0F (316^0C), above product use specifications, will undergo some thermal cracking [e.g. removal of long alkyl chains, making aromatic compounds smaller and more bioavailable], generating more PAC in fume. Longer duration heating at or above 450^0F (232^0C) may lead to volatilization of constituents not found in field samples, and possible chemical reactions that do not occur in field operations (AI, 1990a), producing a fume not comparable to "real world" material. Chemical characterization of roofing fumes in the Niemeier et al., (1988) study have been shown to bear little resemblance to the fumes collected at field paving and roofing sites (McCarthy et al., 1999). For almost a decade, the Heritage Research Group and the Fraunhofer Institute of Technology and Experimental Medicine (Fraunhofer-ITEM) have worked on developing methods to properly collect and characterize asphalt fume condensate samples that mimic real world exposure conditions (Kriech et al., 1999; Kurek et al., 1999; Kriech et al., 2002; Kreich et al., 2004; Kriech et al., 2007; Fraunhofer ITEM 2003; Priess et al., 2006; Pohlmann et al., 2006a,b). Further, Fraunhofer ITEM developed a state of the art fume generation method that has been utilized in testing asphalt fume condensate in subchronic and chronic inhalation studies (Fraunhofer ITEM, 2002a,b; Fraunhofer ITEM, 2003). A similar fume condensate generation method was employed in the recently completed OEDC 422 reproductive developmental study and the OECD 474 micronucleus assay (Fraunhofer ITEM, 2009).

3.2 New Studies

As mentioned previously, the asphalt category is comprised of a single group of six heavy residual streams derived from the high temperature vacuum distillation of petroleum. Two category members, asphalt and oxidized asphalt, represent >99% of all asphalt material end-uses. To obtain test materials representative of current asphalt product specifications and workplace exposure, four samples of the dominant paving asphalt grade [PG 64-22] were selected. These samples represented four different crude oil slates and were obtained from four different geographical regions of the US. Similarly for the oxidized asphalt, four Type III roofing asphalts were selected from 4 different prominent crude oil slates and different geographical regions. Type III Built Up Roofing asphalt was chosen for this study because it is the most widely used hot field applied roofing asphalt in the US. The asphalt used to make asphalt shingles is used at in greater volumes but this roofing material is applied cold in the field and in manufacturing the exposures are quite low. Therefore the Type III was chosen for its prevalence and potential for worker exposure. Paving-worker industrial hygiene (IH) samples and roofing-worker IH samples were obtained from each of the asphalts. Mannequins were placed at points where particularly high fume concentrations were expected to obtain additional data at higher concentrations to qualitatively guide the collection and characterization of fume to mimic real-world exposure scenarios (Kriech et

al., 2006; Kriech et al., 2007). Asphalt fume condensates were collected using the same protocol that the Fraunhofer Institute of Technology and Experimental Medicine (Fraunhofer-ITEM) employed in a recent chronic inhalation study (Priess et al., 2006; Pohlmann et al., 2006a,b). This involved collecting fume from the headspace of storage tanks, cooling and condensing the fume and storing it in vacuum containers. Fume condensate samples were analyzed for compositional similarity to material to which workers might be exposed as defined by the IH sampling program described above. Parameters included particle size monitoring, boiling point distributions, fluorescence analysis, and qualitative comparison between individual PAHs and selected extracted ions from gas chromatography/mass spectroscopy (GC/MS) analysis. Finally, an Optimized Ames Test[1], was conducted on each of the test materials to compare relative biological activity between samples. Paving samples from the 4 different crude sources were qualitatively similar to each other in a number of the analytical tests performed. Roofing fume samples from the 4 different crude sources were also qualitatively similar.

Since increased temperature is known to directly affect both the quantity and physical-chemical properties of the fume (including PAH content), a single oxidized asphalt roofing fume sample was chosen as the test material for new studies since it had the higher collection temperature and presented a greater potential for a possible health effect. Protocols and acceptance criteria for sample selection and characterization were reviewed and approved by an independent scientific advisory committee (Kriech et al., 2006; Kriech et al., 2007). Fraunhofer ITEM then conducted an OEDC 422 subchronic and reproductive developmental study and OECD 474 micronucleus test using this oxidized roofing fume sample. (Fraunhofer ITEM, 2009).

[1] The Optimized Ames test optimizes exposure of insoluble petroleum substances to *Salmonella typhimurium* to evaluate mutagenicity [see ASTM Method E1687-95]. The method involves extraction of the test material to concentrate condensed ring aromatic hydrocarbons (PAC), alteration of the rodent liver activating system to maximize metabolism and testing in *Salmonella* strain TA98, the strain most sensitive to PAC. Mutagenic activity is reported as the Mutagenic Index [MI], the slope of the initial linear portion of the dose response curve [revertant/µL]. Oils with MI<1.0 are unlikely to be dermally carcinogenic; oils with MI>1.0<2.0 are marginal and MI>2.0 are likely dermal carcinogens.

4. PHYSICAL-CHEMICAL PROPERTIES

4.1 Physical-Chemical Screening Information Data Set (SIDS)

Because the HPV substances covered under the testing plan are mixtures of differing compositions, it is not possible to measure or calculate a single numerical value for some of the physicochemical properties. For example, a complex substance does not have a melting point, but rather a melting point range. Therefore, values for some physicochemical properties will be represented as ranges of values according to the composition of the complex substance. Although some data for substances in this category exist, not all of these endpoints are defined and a consensus database for chemicals that are constituents of complex substances in this category does not exist. Therefore, calculated and measured representative data are identified and a technical discussion is provided where appropriate. The EPIWIN© computer model (US EPA 2000), as discussed in the US EPA document entitled "The Use of Structure-Activity Relationships (SAR) in the High Production Volume Chemicals Challenge Program" is used to calculate some of the physical/chemical properties of representative constituents for selected production streams within the Asphalts Category.

The physical-chemical endpoints in the HPV chemicals program include the following:

- Melting Point
- Boiling Point
- Vapor Pressure
- Octanol/Water Partition Coefficient
- Water Solubility

4.1.1 Melting Point

Asphalts are viscoelastic substances without sharply defined melting points (ASTM 2006). They gradually become softer and less viscous as the temperature rises. For this reason, the softening point is commonly used as a means of standardizing the classification of the flow characteristics of asphalts (ASTM 2006). By this method, asphalt is placed into a vessel of specified dimensions and suspended in a water bath. A standardized steel ball is placed at the center of the sample and the water bath is heated at a controlled rate. The temperature at the instant the steel ball reaches the bottom of the vessel is recorded as the softening point.

A range of softening points, as measured by ASTM Method D36, of a penetration grade (CAS No. 8052-42-4), a hard grade (CAS No. 8052-42-4) and an oxidized grade (CAS No. 64742-93-4) of asphalts were reported by CONCAWE (1992) as 30 to 60 °C, 60 to 75 °C and 60 to 130 °C, respectively.

4.1.2 Boiling Point

Asphalt and vacuum residuum are obtained as the residues from the vacuum distillation of crude oil. CONCAWE (2001) reported a typical boiling range of >450 °C. This is consistent with values given in CONCAWE (1992) and API (1987) for asphalts and bitumens.

4.1.3 Vapor Pressure

Substances in the asphalt category are semi-solid to solid, boil at temperatures above 450^0C, and have negligible vapor pressures at ambient temperatures (CONCAWE 2001). The vapor pressures of representative hydrocarbon structures covering the range of carbon numbers typically found in substances in the asphalt category (e.g., 25 to 50 C atoms) were estimated. The estimates were found to be generally lower than measured values to the extent that they can be determined using standard testing methods. For generic hydrocarbon structures representing paraffinic, naphthenic, and aromatic compounds having 25 carbon atoms, modeled vapor pressure values ranged from 4×10^{-12} hPa to 2×10^{-6} hPa, while the values for hydrocarbons with 50 carbon atoms ranged from 7×10^{-19} hPa to 2×10^{-6} hPa.

Although the production of asphalts removes the majority of hydrocarbons that boil below 1000^0C (see Appendix B), some hydrocarbons having fewer carbon atoms than those typically found in asphalts may exist in the solid matrix at very low concentrations. Those constituents may have measurable vapor pressures when they exist in their pure form, but they are not volatile when they are entrained in the asphalt matrix. However, some of these more volatile hydrocarbons may have the opportunity to escape the asphalt matrix when heated during roofing and paving applications.

Vapor pressures for representative constituents that are present at low concentrations in asphalt fume are included in the Robust Summaries.

4.1.4 Partition Coefficient

Substances in the asphalt category are semi-solid to solid at ambient temperatures and have negligible vapor pressures and water solubilities (CONCAWE 2001). Estimating the partition coefficients of representative hydrocarbon structures having 25 carbon atoms using the EPIWIN computer model (US EPA 2000) showed partition coefficients to be typically >10. Therefore, these complex substances will not exhibit measurable partition coefficients when assessed in standard testing methodologies (OECD 1993). Some hydrocarbon constituents with carbon numbers that fall below the typical asphalt range may have measurable partition coefficients in their pure state, but as constituents in the asphalt matrix their contribution to this property will not be measurable.

4.1.5 Water Solubility

Substances in the asphalt category consist of hydrocarbons having 25 or more carbon atoms and molecular weights of 500 to 2000. At room temperature, these substances exist as semi-solid to solid materials and as such they are expected to have extremely low water solubility (CONCAWE 1992, 2001). However, since substances in this category are often employed in waterproofing applications (NIOSH 2000), there is a potential to leach components from the asphalt into the water.

Brandt and De Groot (2001) studied the PAH compounds in static aqueous leachate water from nine bitumens (asphalts). They found trace amounts of petroleum hydrocarbons, naphthalene being the most prevalent with concentrations ranging from 0.9 to 371 ng/l (parts per trillion). Concentrations of higher ringed PAHs were substantially less. In another study; Kriech (1990) measured a series of PAH compounds in aqueous leachate using fresh hot-mix asphalt. Only naphthalene was quantified at 250 ng/l. All other PAH compounds were below the detection limits for the analyses (detection limits ranged from 15 – 194 ng/l). While the water solubility values of PAH components (i.e., for the pure substance) have been added to the robust summary for reference, these do not reflect the solubility of asphalt as a whole.

Kriech (1990) also analyzed the aqueous leachate for eight metals. All but chromium were below detection limits for the analysis. Detection limits ranged from 0.005 mg/L (As, Se, Hg) to 2 mg/L (Ba). Chromium measured 0.1 mg/l, but was considered by the author to be a result of sample contamination (Kriech 1990; Kriech 1992).

Kriech, et al. (2005) conducted a Toxic Characteristic Leaching Procedure (TCLP) on 10 asphalts [6 paving and 4 roofing asphalts] and analyzed for 22 metals. When samples were crushed and pulverized and tumbled in pH 2.88 water for 18 hours, titanium and zinc were detected in all 10 samples at an average of 23 and 64 µg/l (parts per billion), respectively. Eleven metals were not detected in any sample, while the remaining metals were detected in one or more of the samples at an average concentration near the range of the reported detection limit (4 to 10 µg/l). Aluminum measured 56 µg/l, but the authors acknowledged contamination in the procedure.

4.2 Assessment Summary for Physical-Chemical Endpoints

The physical-chemical characteristics of the members of the Asphalt Category show that these substances are solid to semi-solid viscoelastic substances with extremely high boiling temperatures (>450 °C). They have negligible vapor pressures. Partition coefficients for hydrocarbons representing the typical range of carbon numbers cited for these substances were estimated to be typically >10. Asphalt is essentially insoluble in water due to the high molecular weights of the component hydrocarbons. Any leaching of minor lower molecular weight constituents was shown to be slight or not detectable.

5. ENVIRONMENTAL FATE

5.1 Environmental Fate Endpoints

To assess the environmental fate properties for the HPV program, the U.S. EPA has selected important fate endpoints by which these substances may be characterized. Thus, environmental fate endpoints include the following**:**

- photodegradation,
- stability in water (hydrolysis),
- environmental distribution (fugacity), and
- biodegradation.

5.1.1 Photodegradation

Asphalt and other compositionally similar materials found in this category are composed of high molecular weight hydrocarbon molecules containing 25 or more carbon atoms. At ambient temperatures these substances exist as semi-solid to solid, having negligible vapor pressures and water solubility's. These physical/chemical properties limit their distribution in the environment. Although constituent hydrocarbons present in the asphalt process streams in this category are not expected to partition to air or dissolve in water, when heated during road-surfacing and roofing applications, fumes and vapors are created (NIOSH 2000). Fumes will condense when cooled, but residual vapor may be transported and dispersed in the atmosphere. When this occurs, any hydrocarbon molecules which are liberated from the asphalt matrix may undergo direct or indirect photodegradation depending on the extent to which they are transported and their exposure to conditions conducive to those reactions.

5.1.1.1 Direct

Some asphalt constituents are polyaromatic compounds, which have been shown to absorb light energy in the 290 to 800 nm range where direct photolytic reactions may result. However, absorption is not always sufficient for a chemical to undergo photochemical degradation. The degree and rate at which these compounds might engage in direct photodegradation reactions depend upon penetration of light with sufficient energy to effect a chemical change.

5.1.1.2 Indirect

Indirect photodegradation may occur in the atmosphere when organic compounds interact with photochemically produced hydroxyl radicals, ozone or nitrogen oxides. Saturated hydrocarbon compounds react readily with OH and NO_3 radicals, and monoaromatic and diaromatic compounds react with OH radicals to undergo degradative reactions (Atkinson 1990).

Estimated half-lives of representative hydrocarbon structures covering the range of molecular weights known to exist in asphalts ranged from 0.1 to 0.4 days. Half-lives of specific polyaromatic hydrocarbons were estimated to be 0.2 to 1.2 days. Although individual hydrocarbon molecules present in the asphalt category have the capability to undergo direct or indirect photodegradation reactions, the significance of this fate process is expected to be minimal. At ambient temperatures, these materials will exist as semi-solid to solid substances with negligible water solubility and vapor pressure thus limiting their dispersal and photodegradation in the environment. However, if conditions exist whereby any vapors are released, the estimated data show a low likelihood of atmospheric persistence.

5.1.2 Stability in Water

Hydrolysis of an organic chemical is the transformation process in which a water molecule or hydroxide ion reacts to form a new carbon-oxygen bond. Chemicals that have a potential to hydrolyze include alkyl halides, amides, carbamates, carboxylic acid esters and lactones, epoxides, phosphate esters, and sulfonic acid esters (Harris 1982). Materials in the Asphalts HPV Category are not subject to hydrolysis.

5.1.3 Transport between Environmental Compartments

Substances in the Asphalt HPV Category contain some of the heaviest and least volatile fractions of petroleum (US EPA 1985). At ambient temperatures they exist as semi-solid to solid substances with negligible vapor pressure and negligible water solubility. These physicochemical characteristics of these substances limit their capacity to distribute to different environmental media. Although the vast majority of hydrocarbon molecules are C25 and higher, small amounts of low molecular weight polyaromatic hydrocarbons (PAHs) have been measured in solid asphalt materials (API 1987; CONCAWE 1992). Concentrations of these substances in asphalt and vacuum residue are extremely low (typically in the parts per trillion range) and under normal ambient conditions trapped in the asphalt matrix. When heated, as occurs in road building and roofing applications, asphalt products emit fumes and vapors that contain mixtures of aliphatic and aromatic hydrocarbons (NIOSH 2000). As fumes and vapors cool, the fumes condense onto local surfaces or collide and stick together with further precipitation from the air (NIOSH 2000), which limits the transport from the site of origin. Vapors of aliphatic and aromatic hydrocarbons which remain suspended have the potential to undergo direct and/or indirect photodegradation in accordance with the molecule's capacity to react and the conditions that permit those reactions to occur.

5.1.4 Biodegradation

Biodegradation is the utilization of a chemical by microorganisms as a source of energy and/or carbon. The parent chemical is broken down to simpler, smaller chemicals, which are ultimately converted to an inorganic form such as carbon dioxide, nitrate, sulfate, and water. Assessing the

biodegradability of chemicals using a standard testing guideline can provide useful information for evaluating chemical hazard. Biodegradation can be measured using the OECD test guidelines 301A-F or 302A-C (OECD 1993). However, because of their structures and physical states, biodegradation rates of materials in the Asphalt category would not be measurable using standard testing guidelines. However, substances in this category have shown some susceptibility to biodegradation by a few microbial species. Various microorganisms have been isolated that are able to utilize asphalt as a source of carbon for growth. For example, Phillips and Traxler (1963) demonstrated that species of *Pseudomonas, Chromobacterium*, and *Bacillus* were capable of degrading thin films of asphalt painted on culture flasks. Degradation between 3 and 25% were measured after one week of incubation, and in one experiment measured 90% after one month. Fluctuations in temperature, pH, and oxygen tension affected to a greater or lesser degree the ability of these microorganisms to biodegrade asphalt (Phillips and Traxler 1963; Cundell and Traxler 1973).

Although hydrocarbon components in asphalt appear capable of being biodegraded, degradation rates are greatest under laboratory conditions where the surface area available for microbial contact was maximized and other physicochemical conditions optimized for greatest effectiveness (ZoBell and Molecke 1978). Under realistic exposure conditions, where the bulk properties of asphalt limit dispersion and the available surface area for microbial exposure, biodegradation is expected to be minimal.

5.2 Assessment Summary for Environmental Fate

At ambient temperatures substances in the Asphalt Category exist as semi-solid to solid materials having negligible vapor pressure and water solubility. These physical/chemical features limit their distribution to different environmental compartments. Therefore, asphalts will tend to remain within the terrestrial or aquatic compartment to which they were released. During the applications of asphalts, fumes may be generated when the material is heated, and these fumes may condense onto local surfaces as they cool. Any vapors that remain suspended have the potential to interact with tropospheric OH radicals, and in this manner indirectly photodegrade within a matter of hours to a few days. Although hydrocarbons can be utilized as an energy source by microorganisms, asphalts would not dissolve or disperse in a manner to augment microbial attack. Due to the bulk properties of asphalt, a release to the environment would not result in measureable biodegradation.

6. ENVIRONMENTAL EFFECTS

6.1 Aquatic Toxicity

The environmental effects endpoints in the HPV Challenge program include:

- Acute Toxicity to Fish,
- Acute toxicity to Aquatic Invertebrates, and
- Toxicity to Algae (Growth Inhibition).

There are no standard testing guideline studies on the toxicity of asphalt or vacuum residue to these aquatic organisms, but contaminants in surface water runoff from in-place pavements have raised questions concerning potential environmental impacts to receiving water bodies (Buckler

and Granato 1999). Trace chemical analyses have shown that runoff from pavements contains a multitude of chemicals including deicers (Adams-Kszos *et al,* 1990; Crowther and Hynes, 1977), metals (Maltby *et al*. 1995; Adams-Kszos *et al*. 1990; Moore and Butler 1994), and organic compounds (Dupuis *et al*. 1999; Maltby *et al*. 1995; Horner and Mar 1985). However, these chemicals typically originate from vehicle emissions, spills/droppings of crankcase oil, deicers, nutrients, pesticides/herbicides, fuel additives, maintenance materials and catalytic converter emissions (Buckler and Granato 1999). Hence, adverse impacts to water bodies receiving pavement runoff are likely to result from those types of constituents rather than from leachate from asphalt itself. In fact, studies have shown non-detected or very low concentrations (e.g., ng/l levels) of hydrocarbons and inorganic elements originating from asphalt leachate (Asphalt Institute 2003; Brandt and De Groot 2001, Kriech et al., 2005).

Asphalt and vacuum residuum are not expected to cause acute or chronic toxicity to aquatic organisms due to the extremely low water solubility of these substances. Asphalt linings have been applied to aquaculture ponds in Oregon and Washington with no apparent adverse impact to the culture and propagation of sport and food fish (Schlect 1991). Evidence for a lack of aquatic toxicity also is shown using data on other petroleum streams having similar types of hydrocarbon constituents (i.e., saturated and aromatic fractions). For example aromatic extracts of vacuum distillates, produced during manufacture of lubricant base oils, contain a large proportion of polyaromatic hydrocarbons of C20 – C50. These aromatic extracts showed no acute or chronic toxicity in aquatic organisms (CONCAWE 2001). Similarly, lubricating oil basestocks, which contain saturated hydrocarbon constituents as well as small quantities of aromatic hydrocarbons of C15 – C50, showed no acute or chronic toxicity to aquatic organisms (CONCAWE 1997; API 2003). These data are shown in Table 3, below. All studies cited in Table 3 employed exposure solutions prepared as water accommodated fractions (WAFs) in accordance with OECD recommendations for testing complex substances having low water solubility (OECD 2000). Asphalt and vacuum residuum, with saturated and aromatic hydrocarbon molecules of C25 and higher, also are not sufficiently water soluble to elicit acute or chronic toxicity in aquatic animals and plants.

Table 3. Representative Ecotoxicity Data for Lubricating Base Oils and Aromatic Extracts.

	Fish Acute/Prolonged Toxicity	Invertebrate Acute Toxicity	Algal Toxicity	Invertebrate Chronic Toxicity
Lubricating Base Oils[1] C15-C50	96-hour LL0 = 1000 mg/L 7-day LL0 = 1000 mg/L	48-hour EL0 = 1000 mg/L	96-hour NOEL = 1000 mg/L	21-day NOEL = 1000 mg/L
Aromatic Extracts [2] C20 - C50	96-hour LL0 = 1000 mg/L	48-hour EL0 = 1000 mg/L	72-hour NOEL = 1000 mg/L	21-day NOEL = 1000 mg/L

(E)LL0 = Test substance loading concentration at which no mortality or effects existed.
NOEL = No observed effect level.
[1] CONCAWE 1997
[2] CONCAWE 2001

6.2 Assessment Summary for Environmental Effects

The constituent hydrocarbons making up asphalt and vacuum residuum are of such high molecular weight and low solubility that such substances would not be expected to cause acute or chronic toxicity to aquatic organisms. This is supported by data from other petroleum streams having similar hydrocarbon structures.

7. HUMAN HEALTH ENDPOINTS

Toxicity data has been developed from both whole asphalt and asphalt fumes. Previous laboratory studies have focused primarily on the carcinogenic properties of asphalt and asphalt fumes using carcinogenesis tests as well as genetic toxicity studies. To fulfill its obligations under the HPV program, the API determined that some testing needed to be conducted to assess certain specific endpoints. The API also determined that, due to its physical and chemical properties, testing of asphalt per se would be difficult and that results of tests of asphalt would be of limited value in assessing its potential hazards. Accordingly, the API concluded that it would be more sensible to test a substance which represents the material to which humans would be exposed. The API understands that exposure to asphalt occurs primarily during roofing and paving applications; in these situations the asphalt is heated to allow it to be applied, this results in the production of asphalt fumes which constitute the principal route of human exposure; accordingly for purposes of this program, the API determined that the most useful tests to be conducted would be by inhalation exposure to asphalt fumes. Fume generation represented its own challenges. The API relied on industrial hygiene surveys of roofing asphalt workers to characterize the composition of the fume to which humans would be exposed occupationally and then prepared a test sample which was a close match in terms of physical and chemical properties. This sample was then used to in the API HPV program to assess the potential for repeated dose toxicity, reproductive effects, and, to some effects, genetic toxicity. Results of other programs with similar test materials provide other information on repeated dose testing including chronic toxicity and carcinogenicity testing as well as additional information on potential mutagenic effects.

Detailed study information is available in the Robust Summaries organized in the IUCLID data set format and HPVIS format (Appendix E). The data submitted to the HPV program has been developed with the goal of facilitating international harmonization of hazard and risk characterization worldwide.

7.1 Human Health Effects

7.1.1 Acute Toxicity

7.1.1.1 Oral and Dermal

Acute oral toxicity studies on two vacuum residuum samples, API 81-13 and API 81-14 [CAS #647-56-6] (API 1982a, b) demonstrated that asphalts did not induce significant acute toxicity by the oral route in rats [LD50 >5.0g/kg] although hypoactivity, diarrhea and dark staining of the anal region

were observed. Samples were administered to Sprague Dawley rats [5/sex] at 5g/kg in corn oil in single oral doses and animals were monitored hourly for the first six hours post-treatment and twice daily for 14 days. Body weights recorded at 7 and 14 days indicated that growth was unaffected by treatment with either material.

In dermal toxicity tests, undiluted vacuum residuum samples were applied at 2.0g/kg to the shaved backs of New Zealand White rabbits [2 abraded, 2 non-abraded/sex] and covered with an occlusive dressing. After 24 hours, the dressings were removed and the skins were wiped. Animals were monitored hourly for the first six hours post-treatment and twice daily for 14 days. No mortality or visible lesions were observed at necropsy. [LD50 >2.0g/kg].

7.1.1.2 Inhalation

Male and female Wistar WU rats were exposed to fumes generated from condensate collected in the headspace of a bitumen storage tank, by nose-only inhalation for 4.5 hours according to OECD guideline 403 at a target concentration of 100mg/m^3 (Fraunhofer ITEM, 2000). Mean actual exposures measured by IR spectroscopy according to BIA (Germany) guideline #6305 were 26mg/m^3 for the first 30 minutes and 182mg/m^3 for the subsequent 4 hours. No mortality or toxicity was observed, except for slightly lower body temperatures at the end of exposure. Therefore the LC50 was > 182mg/m^3. It should be noted, however, that in other tests rats were exposed repeatedly to asphalt fume condensate at levels up to 300 mg/m^3 without evidence of lethality or profound toxic effects.

7.1.1.3 Skin and Eye Irritation

In rabbits, slight dermal irritation was observed [Irritation Index = 0.2 for API 81-13; 0.4 for API 81-14] after application of 0.5ml vacuum residuum to two areas of the skin [1 area abraded, 1 unabraded] of 6 male New Zealand rabbits (API, 1982a,b). Sites were covered with occluded dressings for 24 hours. Immediately after removal of dressings the erythema and edema scores were determined using the Draize scale, and scored again at 72 hours, 96 hours, 7 days and 14 days after removal of the dressings.

Mild to moderate eye irritation in both washed and unwashed eyes was observed at 24 hours (API, 1982a,b) in 9 New Zealand White rabbits exposed to 0.1ml undiluted test material. Thirty seconds after instillation, the eyes of 3 rabbits were flushed; the eyes of the other 6 rabbits were not washed. Eyes were examined at 1, 24, 48, 72 hours and 7 days post-exposure. Eye irritation was maximal at 24 hours [PII = 4.0 in unwashed eyes and 5.3 in washed eyes] which diminished over time to PII = 0 at 7 days.

7.1.1.4 Sensitization

Dermal treatment of guinea pigs with undiluted, heated vacuum residuum samples (API 81-13; API 81-14) did not induce sensitization in the Buehler test (API, 1984a, b).

7.1.1.5 Human Effects

Acute effects among construction field workers exposed to asphalt fumes included eye irritation, and nasal and throat irritation which typically appeared to be of mild severity and were transitory in nature (Gamble et al., 1999; NIOSH, 2000). Dermal exposure to neat asphalt formulations is limited, in that these materials are handled hot (180-450^0 F) and even brief exposure will cause

immediate skin burns. Skin irritation has also been reported after human exposure to asphalt based materials (cold product or fume) but these results may be confounded by co-exposure to diesel fuel, coal tar or fiberglass, and environmental conditions (Chase, 1994; Tavris et al, 1984; NIOSH, 2000).

Conclusions: Results of animal studies and human monitoring indicate that acute toxicity of asphalts and asphalt fumes is low and effects are transitory. Asphalts cause slight dermal irritation and mild to moderate eye irritation but are not skin sensitizers.

7.1.2 Repeated Dose Toxicity

Oxidized roofing asphalt fume condensate, [CAS # 64742-93-4, RAFC] was tested by nose-only inhalation in an OECD 422 Combined Repeated Dose Toxicity Study with the Reproductive/Developmental Toxicity Screening Test also containing an OECD 474 Micronucleus assay (Fraunhofer ITEM, 2009). General study procedures and the result of the systemic repeated dose segment are presented here. Details of the reproductive/developmental segment are found in Section 7.1.5 and OECD 474 Micronucleus assay in Section 7.1.4. RAFC fume was delivered through stainless steel tubes to male and female Wistar (Crl:WU) rats housed in acrylic glass tubes at target concentrations of 0, 30, 100 and 300 mg/m^3 total hydrocarbons (THC) for 28 days to subchronic animals and up to 42 days for pregnant females. Actual mean concentrations measured continuously throughout the entire exposure period by aerosol photometers were 0, 30.0, 100.1, and 297.3 mg/m^3 THC. In addition to measurement of standard toxicity parameters, spermatology and neurobehavioral endpoints [locomotor activity and functional observational battery] were evaluated at study termination. Body weight gain and food consumption were significantly reduced in high dose males. No test material-related effects were seen in body weight gain or food consumption in females. Statistically significant differences from controls in absolute body weight of females were reported but were more likely due to an error in the randomization program at study initiation than to treatment. Water consumption was unaffected in males and females of all groups compared to controls. No treatment-related adverse effects were reported for hematology or clinical chemistry endpoints. No adverse effects were observed in neurobehavioral performance. Sperm motility and percent abnormal sperm in treated groups were comparable to controls. Sperm count showed a dose-related but non-significant decrease in exposed groups but all values were within historical control parameters for this laboratory. Absolute and relative lung weights were increased in high dose males. Absolute lung weights were statistically significantly increased in all subchronic females and mid and high dose breeding females. Relative lung weights were statistically significantly increased in mid and high dose subchronic females and in high dose breeding females. Absolute liver weights demonstrated dose-dependent increases in all subchronic females with statistical significance at 297.3mg/m^3 but no statistically significant relative liver weight increases were seen. Histopathological changes seen in the nasal cavity consisted of a statistically significant decrease in inflammatory cell infiltrate in high dose subchronic animals of both sexes in contrast to slight inflammatory cell infiltrate in nasal tissue of breeding females at 297.3 mg/m^3. Minimal adverse effects consisting of slight increase in alveolar macrophage accumulation in combination with minimal mononuclear/inflammatory cell infiltration and slight adaptive alveolar hyperplasia were seen in the lungs of animals in the 297.3 mg/m^3 group but not at 100 or 30 mg/m^3 exposure levels. For males, LOAEL = 297.3 mg/m^3 based on decreased body weight gain, decreased food consumption and changes in lung parameters, and NOAEL = 100 mg/m^3. For females, LOAEL = 100 mg/m^3 based on changes in lung histology parameters, and NOAEL = 30 mg/m^3.

Inhalation (nose-only) exposure of male and female Wistar (Crl:WU rats) [16/sex/group] to asphalt fume condensate (CAS #8052-42-4) collected over a paving asphalt tank was performed for 90 days at target concentrations of 0, 4, 20, and 100 mg/m^3 according to OECD guideline 413 (Fraunhofer ITEM, 2001). Actual mean concentrations measured by IR according to BIA [Germany] guideline #6305 and corrected for aromatic content (Ekström et al., 2001), were 5.53, 28.17, and 149.17 mg/m^3 total hydrocarbon of bitumen fumes. At 149.17 mg/m^3, male rats exhibited statistically significant lower body weights with a concurrent decrease in food consumption, and female rats had slightly lower body weights than controls. Histopathological changes were observed in the nasal and paranasal cavities in both sexes consisting of slight to moderate occurrence of hyalinosis and some mucosal cell hyperplasia in the highest exposure group. Broncho-alveolar lavage demonstrated a statistically significant increase in mean cell concentration, lactate dehydrogenase levels and alpha glutamyl transferase levels in high dose female rats; effects in high dose males were similar but less pronounced. For this study the LOAEL was 149.17 mg/m^3 and the NOAEL was 28.17 mg/m^3

In two dermal toxicity studies, New Zealand White rabbits [5/sex/group] were treated with 200, 1000, and 2000 mg/kg vacuum residuum samples API 81-13, API 81-14, undiluted and occluded, once a day for 6 hours, 3 times a week for 4 weeks. At 2000 mg/kg, rabbits appeared thin, experienced decreased body weight gain, and decreased food intake. Flaking skin, acanthotic dermatitis and hyperkeratosis were seen in males given 2000 mg/kg API 81-13, and API 81-14 also produced wart-like lesions and white discharge at the treated site in both sexes. No treatment-related systemic toxicity was reported (API, 1983a, b).

Conclusions: Nose-only inhalation exposure of rats to roofing or paving asphalt fume condensate over durations of 28 to 90 days, respectively resulted in a similar range of LOAEL values of 149.17 to 297.3 mg/m^3 and NOAELs of 28.17 to 30.0 mg/m^3. Overall effects were decreased body weight gain and food consumption. Effects on the respiratory system included increased lung weights and slight to moderate histopathologic changes in nasal cavities and lungs at the highest exposure levels (approximately 300 mg/m3). In dermal exposure to asphalt, toxicity was seen primarily at the application site; there was no evidence of systemic effects. Overall asphalt and asphalt fume condensates do not induce profound systemic toxicity at tested doses.

7.1.3 Genetic Toxicity *In Vitro*

7.1.3.1 Bacterial Assays

The testing of whole asphalts diluted or extracted with organic solvents resulted in no mutagenic or weak mutagenic activity only with metabolic activation (rodent S-9 liver homogenate) in *Salmonella typhimurium*. Penalva et al. (1983) found weak activity for a dimethyl sulfoxide (DMSO) extract of road tar (that may have contained coal-derived material) with S-9, while Monarca et al (1987) reported that DMSO extracts of three asphalt samples were not mutagenic in the *Salmonella* assay, nor were extracts from airborne particulates collected during road paving operations, even using a 5-fold increased S-9 mixture. Four samples of asphalt-based paints [60% asphalt cut back with mineral spirits] were inactive in *Salmonella* with or without S-9 microsomal activation (Robinson et al., 1984).

Blackburn and Kriech (1990) reported marginally positive findings with DMSO extracts of roofing and paving asphalts in the Optimized Ames Test [ASTM method E1687-95], using elevated levels of S-9. Fume condensates, derived from heating these asphalts to temperatures greater than 232^{0}C (450^{0}F) were moderately active, and comparably generated fumes from coal tar pitch were greater than 1000 times more active. When paving asphalt was heated to a temperature more representative of that in recommended use, 163^{0}C (325^{0}F), very little fume was generated and mutagenic activity was much lower.

The National Toxicology Program evaluated the mutagenic potential of asphalt fume condensates and fractions prepared by Sivak et al. (1989) for dermal carcinogenicity studies, by heating Type III roofing asphalt to 316^{0}C (601^{0}F) to generate fumes. The fumes were fractionated into 5 fractions (A-E) using HPLC. The unfractionated fume condensate and fractions B and C [containing PAC] were weakly positive; fraction E, comprised primarily of C6-C22 alkylated ketones, alkylated naphthols and phenols, was negative, and the recombined A-E fraction was positive with metabolic activation (NTP, 1990). The same fractions tested by Blackburn and Kriech (1990) gave similar results using the Optimized Ames test.

Machado et al. (1993) evaluated the mutagenic activity and PAH content of laboratory generated fumes from two Type III roofing asphalts from different crudes [fumes generated at 232^{0}C (450^{0}F) or 316^{0}C (601^{0}F)], 18 paving asphalts from 14 different crude oil sources and various processing conditions [fumes generated at 163^{0}C (325^{0}F)], and one Type I coal tar pitch [fumes generated at 232^{0}C (450^{0}F) or 316^{0}C (601^{0}F)]. All asphalt samples showed weak to moderate mutagenic response in the Optimized Ames Test, responses approximately 100-fold less than the mutagenicity of the coal tar pitch sample.

Reinke and Swanson (1993) and Reinke et al., (2000) also compared chemistry of PAH and sulfur containing PAC and mutagenic potential in the Optimized Test, of field and laboratory generated asphalt fume condensates from asphalt cement. Field samples were collected from headspace of an asphalt storage tank at 146-157^{0}C (295-315^{0}F) and laboratory samples were generated at 149^{0}C or 316^{0}C. Field samples were not mutagenic [MI<1] whereas laboratory fumes generated at 149^{0}C [MI 5.3][1] and 316^{0}C [MI 8.3] were clearly mutagenic [MI>2]. Authors noted positive trends between mutagenicity and the percentage of 3-ring and greater PAH and S-PAC, and postulated that the higher mutagenicity of fumes generated at 316^{0}C could be attributed to increased concentration of 4-ring S-PAC.

DeMéo et al. (1996) made similar comparisons in the Optimized Ames Test for fumes of coal tar and two paving asphalts generated at 160^{0}C and 200^{0}C (320^{0}and 392^{0}F), and found all fumes mutagenic in *Salmonella* with metabolic activation. Coal tar fume condensates induced mutagenic effects with MI values that were 15-600 fold higher than that of asphalt fume condensates. All fume condensate samples also induced DNA adducts in calf thymus DNA *in vitro*. No specific adducts were identified and the pattern of autoradiograms of DNA demonstrated qualitative differences in the nature of adducts induced by asphalt or coal tar fume condensates.

The Testing Group collected fumes from the predominant grade of paving asphalt and the predominant grade of roofing asphalt in the USA under realistic end-use temperatures and

[1] MI is an abbreviation for Mutagenic Index. This is a measure of mutagenic potency, measured in the optimized Ames test. The MI values are calculated from the slopes of the dose response curves, and given in units of revertants per ul extract. Mutagenic index values of 2.0 or greater are correlated with dermal carcinogenic activity in the mouse (ASTM, 1995).

compared their bacterial mutagenicity in the Optimized Test (Kriech 2006). Fume condensate from these two samples showed minimal mutagenic activity in the modified Ames test (MI equaled 0.8 and 1.2, respectively).

7.1.3.2 Mammalian cell mutation assays:

Two vacuum residuum samples (API 81-13, API 81-14; CAS #64741-56-6) were solubilized in DMSO and tested in the L5178Y Mouse lymphoma cell mutagenesis assay. Both vacuum residuum samples were not mutagenic without metabolic activation but were weakly active in the presence of S-9 mixture in the range of low to moderate mammalian cell toxicity (API, 1984c, d).

7.1.3.3 Cytogenetic assays

Condensates of Type I and Type III roofing asphalt fumes, and fractions of these condensates generated in the laboratory at 316^0C (601^0F) by the method of Sivak et al. (1989) caused a dose-related increase in micronucleus formation in Chinese Hamster lung fibroblasts (V79) cells (Qian et al., 1996, 1999), primarily by spindle apparatus alteration in dividing cells. However, three paving asphalt fume condensates generated in the field and in the laboratory were negative in a Chinese hamster ovary cell line chromosome aberration assay (Reinke and Swanson, 1993; Reinke et al., 2000).

7.1.3.4 DNA Adducts (Supplemental Information)

Formation of DNA adducts has been used as a biological measure of exposure and potentially as an early step in mutagenicity and carcinogenicity. Extracts of whole asphalt do not induce significant DNA damage, probably because they contain insufficient quantities of biologically active PAH. Hong and Lee (1999) administered a South Korean bitumen extracted in tetrahydrofuran (THF) to HL60 cells and did not observe an increase in DNA strand breaks, DNA cross-linking or formation of reactive oxygen species.

In the ^{32}P- postlabeling assay, asphalt fume condensates [45/60 pen and 160/210 pen] generated at temperature of 160^0 or 200^0C induced formation of DNA adducts in calf thymus DNA with metabolic activation from Aroclor-induced rat liver homogenate at much lower levels than those induced by coal tar fume condensate with a qualitative difference in adducts (DeMéo et al, 1996 – additional information under Sect. 7.1.3.1 bacterial assays). Genevois et al., (1998), also using the ^{32}P-postlabling assay, produced similar results with condensates of bitumen from heavy Venezuelan crude oil [45/60 pen] and confirmed that asphalt fumes stimulate CYP 1A1, the major cytochrome P450 isozyme involved in asphalt metabolism. Akkineni et al., (2001) demonstrated that DNA adducts formed in calf thymus DNA from roofing or paving fumes were at levels comparable to or lower than those induced by a non-carcinogenic, severely hydrotreated naphthenic 100 second base oil.

Conclusions: In vitro genotoxicity

In vitro studies demonstrate that whole asphalts are non-mutagenic or weakly mutagenic, and that fume condensates are mutagenic with the severity of the effect correlated with the temperature under which fumes are generated. DNA adducts have been demonstrated with exposure to asphalt fume condensates at levels comparable to those of a non-carcinogenic oil and lower than those induced by coal tar fume condensate.

7.1.4 Genetic Toxicity *In Vivo*

7.1.4.1 Cytogenetic assays

Vacuum residuum samples (API 81-13, API 81-14) were administered orally to Sprague Dawley rats at doses of 0, 0.3, 1.0, or 3.0g/kg/day for 5 days. No chromosomal abnormalities were seen in bone marrow cells after 5 days of exposure (API, 1983c, d)

Ma et al. (2002) exposed rats intratracheally for 3 consecutive days to asphalt fumes condensates collected at the top of a paving storage tank at a temperature of 160^0C (320^0F) at doses of 0 (saline), 0.45, 2.22 or 8.88mg/kg/day. Exposure to 8.88mg asphalt fume condensate/kg rat body weight caused a statistically significant increase in the level and activity of CYP1A1, a major isozyme of cytochrome P450, in the lung, and increased micronucleus formation in bone-marrow polychromatic erythrocytes (PCE). The incidence of micronuclei was evaluated only at the low and high dose. The increased level of micronuclei at 8.88mg/kg was accompanied by a statistically significant decrease in PCE/1000 erythrocytes, indicative of cell toxicity, which may have affected the micronuclei incidence, and thus potentially confounded results. The investigators attributed the effects to bioactivation of the PAC present in the asphalt fumes. However, the experimental design of this study (only two doses evaluated for micronuclei) and the bone-marrow toxicity observed at the high dose make their interpretation questionable. Also, the use of intratracheal instillations limits comparison to other inhalation studies which have not increased micronucleus frequency (Halter et al., 2007, Fraunhofer ITEM, 2002, Fraunhofer ITEM, 2009).

As part of the 2 year nose-only inhalation carcinogenesis study described below, SPF-Wistar rats were exposed to concentrations of 4, 20 and 100 mg/m^3 total hydrocarbons, 6hr/day for 5 days, 30 days and 12 months. Test material was derived from the overhead space of a hot storage tank of supplied with semi-blown paving bitumen [50/70 pen]. Animals were examined for micronucleated polychromatic erythrocytes in peripheral blood and bone marrow, and DNA adducts [see below Sect 7.1.4.2]. After 5 days, 30 days and 12 months only a few peripheral blood micronucleated erythrocytes were observed and no significant increase in micronuleated cells were seen in bone marrow smears after 12 months (Halter et al., 2007, Fraunhofer ITEM, 2002).

A cytogenetic study following OECD protocol 474 performed for this HPV program as add-on to an OECD 422 protocol in which an oxidized roofing asphalt fume condensate was administered to Wistar [Crl:WU] rats by nose-only inhalation at target concentrations of 30, 100 or 300 mg/m^3 for 28 days did not result in any increase in micronucleated polychromatic erythrocytes in the bone marrow of treated rats compared to control animals (Fraunhofer ITEM, 2009]) Details of exposure are located in the systemic repeated dose section (Section 7.1.2).

7.1.4.2 DNA Adducts (Supplemental Information)

In vivo DNA adduct studies in rats and mice using the ^{32}P-postlabeling technique demonstrated induction of a variety of adducts by asphalt fume condensates but no specific adducts were identified. Genevois et al. (1996) performed an *in vivo* study as a follow-up to the *in vitro* study of DeMéo et al (1996) described above. They demonstrated adduct formation in skin, lungs and lymphocytes of rats dermally treated with asphalt or coal tar fume condensates in different quantities and migration patterns. HPLC analyses of the condensates indicated that coal tar fume condensate contained large amounts of unsubstituted PAH, which were only minor constituents of asphalt fume condensate. Multiple applications of asphalt based paints to the backs of mice

resulted in accumulation of adducts in skin and lung tissue, but again, no specific adducts were identified (Schoket et al., 1988). Qian et al. (1998) using the ^{32}P- postlabeling method, measured DNA adduct levels induced by Type I or Type III roofing asphalt fume condensate instilled in the lungs of male CD rats at concentrations of 250, 500, 1000 or 2000 mg/kg body weight, 3 times at 8 hour intervals. Fume was generated from asphalt heated to 316±10^{0}C by the method of Sivak et al., 1989. DNA adduct levels were increased compared to controls in the lungs of rats treated with Type I asphalt at or above 500 mg/kg, and at 250 mg/kg for Type III asphalt. The migration pattern of DNA adducts was similar for both asphalts. However, there was no elevation in DNA adduct levels in leukocytes collected by cardiac puncture from the same rats. Zhao et al., (2004) reported that whole body exposure of Sprague Dawley female rats to asphalt fumes generated under road paving conditions (120-170^{0}C), 6hr/day for 1-5 days resulted in dose-dependent DNA single strand breaks in alveolar macrophages and lung tissue revealed by the Comet assay. However, no micronucleus formation was seen in bone marrow polychromatic erythrocytes even at very high doses (total maximum exposure of 1733 mg hr/m^3). In studies with transgenic mice (Micillino,et al., 2002) and rats (Bottin et al, 2006) exposed to 100 mg/m^3 total particulate paving asphalt fume [50/70 pen] generated at 170^{0}C, no adduct formation or mutagenic events were seen in mice and only one adduct was identified in the lung of rats with mutant frequency similar between treated rats and controls.

As part of the 2-year nose-only inhalation carcinogenesis study described below, SPF-Wistar rats were exposed to concentrations of 4, 20 and 100 mg/m^3 total hydrocarbons, 6hr/day for 5 days, 30 days and 12 months. Test material was derived from the overhead space of a hot storage tank of supplied with semi-blown paving bitumen [50/70 pen]. Animals were examined for cytogenetic effects [see Sect 7.1.4.1], and DNA adducts using the ^{32}P-postlabeling assay. Halter et al. (2007) identified 3-4 stable DNA adducts in lung, nasal and alveolar epithelium of exposed rats at the mid and high dose levels but no adducts were seen in white blood cells. The level of 8-oxo-dG adduct, a recognized marker for oxidative damage was not increased in any tissue indicating oxidative damage was not a major component of asphalt fume induced DNA effects. Despite the presence of DNA adducts, no tumors were identified in respiratory tissue at the end of the 2-year study.

Representative robust summaries of DNA adduct studies are provided (Qian et al., 1998; Halter et al., 2007)

7.1.4.3 Human Cytogenetic Effects (Supplemental Information)

Cytogenetic results vary and are complicated by co-exposure to other materials such as coal tar fume, diesel exhaust and asbestos as well as life style differences (e.g. smoking). Burgaz et al., (1998) and Murray and Edwards (2005) reported increases in micronucleus formation and/ sister chromatid exchange in peripheral blood of asphalt field workers, but Jarvholm et al. (1999) found no significant increases in pavers exposed to average PAH content of 2.3 mg/m^3. Cavallo et al (2005) identified DNA strand breaks in peripheral lymphocytes of paving workers but no sister chromatid exchanges were observed.

Conclusions: *In vivo* genotoxicity

Oral treatment with vacuum residuum did not cause chromosome damage in treated animals. Asphalt fume condensates administered to laboratory animals by inhalation under realistic fume generation and exposure conditions [e.g. whole body or nose-only] do not induce cytogenetic damage in the respiratory or hematopoetic systems. DNA adducts and strand breaks have been

reported in some systems in the absence of definitive cytogenetic damage expressed as micronucleated polychromatic erythrocytes. However background levels of DNA adduction are essentially universal and it is not clear to what extent low levels of genotoxic damage contribute to human cancer risk (Poirier, 1997). In general asphalt and asphalt fumes are not clastogens in these laboratory assay systems. Human data are highly variable and frequently confounded by co-exposure to other materials.

7.1.5 Reproductive/Developmental Toxicity

Roofing asphalt fume condensate, [CAS # 64742-93-4, RAFC] was tested by nose-only inhalation in an OECD 422 Combined Repeated Dose Toxicity Study with the Reproductive/Developmental Toxicity Screening Test. This was the same study described in greater detail in the systemic repeated dose section (Section 7.1.2; Fraunhofer ITEM, 2009). RAFC fume was delivered through stainless steel tubes to male and female Wistar (Crl:WU) rats housed in acrylic glass tubes at target concentrations of 0, 30, 100 and 300 mg/m^3 total hydrocarbons (THC) for 28 days to male rats and up to 42 days including 2 weeks premating, mating and gestation days (GD) 0-20 for pregnant females. Dams and pups were not exposed to RAFC during 4 days of lactation prior to termination. Actual mean concentrations measured continuously throughout the entire exposure period by aerosol photometers were 0, 30.0, 100.1, and 297.3 mg/m^3 THC. All animals mated within the first 8 days of cohabitation. Reproductive performance of RAFC exposed males was comparable to control rats. No adverse effects were seen in histopathological evaluation of reproductive organs or sperm motility and percent abnormal sperm. Sperm count showed a dose-related but non-significant decrease in exposed groups but all values were within historical control range for this laboratory. Reproductive NOAEL for males = 297.3 mg/m^3. No RAFC-related effects were seen in body weight gain or food consumption in females. Higher body weights of RAFC exposed females compared to controls throughout gestation resulted from randomization error at initiation of study. Overall gestation body weight gain and food consumption were slightly but not statistically decreased in the high dose group. Absolute lung weights were statistically significantly increased at mid and high exposure groups but relative weights were only statistically significantly increased at 297.3 mg/m^3. [Because of the body weight randomization error, only relative organ weight changes are used to determine maternal LOAEL/NOAEL]. Minimal histopathological effects in the 297.3 mg/m^3 THC exposure group occurred in the lungs, where a slight increase of alveolar macrophage accumulation was observed in combination with minimal mononuclear/ inflammatory cell infiltration and minimal to slight (adaptive) alveolar hyperplasia of the bronchiolar type (alveolar bronchiolization). In the nasal cavity, 7/12 rats of the high dose group showed (multi)focal very slight to slight mucosal mononuclear/inflammatory cell infiltration compared to one female control. This effect was not seen in the nasal cavity of subchronic rats. There were no significant RAFC related differences in mean number of pregnant animals, number of animals delivering, mating index, fertility index, or gestation length, number of corpora lutea, number of implantation sites or percent of post implantation loss for any exposure group. Pup viability indices, sex ratio, body weight and body weight gain over lactation days 0-4 were comparable to controls. Maternal systemic NOAEL = 100.1 mg/m^3. NOAEL for reproductive/developmental parameters = 297.3 mg/m^3.

Conclusions: Exposure to oxidized roofing asphalt fume condensate does not induce adverse effects on reproductive or developmental parameters and demonstrates that asphalt fume condensate is not a reproductive toxicant.

7.2 Health Effects Other

7.2.1. Carcinogenicity

Carcinogenicity studies with asphalts include mouse skin painting studies with whole bitumens of different grades or asphalt fume condensates and 2-year inhalation studies with asphalt fumes are summarized in Table 4 (CONCAWE, 1992). Robust summaries of these studies have not been prepared since carcinogenicity is not part of the HPV program. However, a recent nose-only inhalation study considered definitive for inhalation exposure to fume vapor condensate from headspace of a semi-blown paving asphalt (50/70 pen) is described and a robust summary provided (Fuhst et al., 2007).

7.2.1.1. Inhalation Carcinogenicity: Asphalt Fumes

A nose-only inhalation carcinogenesis study was performed at Fraunhofer Laboratories with SPF-Wistar rats[50/sex/group] exposed to concentrations of 4, 20 and 100 mg/m^3 total hydrocarbons paving bitumen fume condensate, 6hr/day, 5 days/week for 2 years [104 weeks] (Fuhst et al, 2007). Actual concentrations were 0, 6.8, 34.4 and 172.5 mg/m^3 calculated by BIA method. Additional control and high dose animals [36/sex/group] were included to investigate cell number, and differential count, total protein, lactic dehydrogenase, ß-glucuronidase and γ-glutamyl-transferase by bronchio-alveolar lavage [BAL], and proliferation of respiratory epithelial tissue, 7 days, 90 days and 12 months. Test material was derived from the overhead space of a hot storage tank of supplied with semi-blown paving bitumen [50/70 pen]. Fumes were representative of the material to which workers are exposed in paving operations. No statistically significant differences were observed in mortality and no clinical signs of intoxication were seen Decreased body weight at study termination was –3% males and –8% females in the 34.4 mg/m^3 group and –7% males and –8% females in the 172.5 mg/m^3 group compared to controls. Statistically significant decreases in body weight gain in the mid and high exposure groups were seen but not at all time points. All hematology parameters measured at terminal sacrifice were in the control range for the species, strain, sex and age. Respiratory effects measured by BAL were slight. Cell proliferation in lung parenchymal cells was comparable to controls and slight increases in the transitional zone of respiratory to olfactory epithelium were seen only in 172.5 mg/m^3 males. Histopathology identified slight dose-related degenerative, inflammatory and proliferative lesions in the nasal cavity and slight dose-related alveolar bronchiolization and mononuclear/inflammatory cell infiltrations in lungs, all indicative of irritant effects. No increases in number of tumor bearing animals were observed and no statistically significant increases in organ-specific tumors were seen in exposed animals compared to controls. NOAEL for carcinogenesis = 172.5 mg/m^3

Two studies were performed in the 1960s; both investigators found evidence of non-specific respiratory irritation in some animals but no evidence of carcinogenicity. Heuper and Payne (1960) exposed Bethesda black rats or Strain-13 guinea pigs to fumes from a roofing asphalt (oxidized bitumen), 5 hr/day, 4 days/wk for 2 years. Fumes were generated by volatilizing air-blown asphalt from a dish heated to 120^0-135^{0}C (250^0-275^{0}F) inside the exposure chamber. None of the animals developed lung cancer but some rats or guinea pigs had chronic fibrosing pneumonitis with peribronchical adenomatosis. Simmer (1964) used a composite sample of asphalts (both steam and air-blown) from 6 different California refineries. The asphalt mixture was comprised of 32% asphaltenes, 32% resins, 14% saturates and 22% aromatics. C57 black mice were exposed to fumes from the pooled asphalt sample heated to 120^{0}C (250^{0}F) for 6-7.5hrs/day, 5 days/wk for 21

months. Histological pulmonary changes included bronchitis, loss of bronchial cilia, epithelial atrophy and necrosis, and pneumonitis. No cancer was induced.

7.2.1.2. Dermal Carcinogenicity

Whole Asphalt

Undiluted penetration grade or oxidized asphalts, heated to make the materials mobile induced a few skin tumors (Simmers, 1965) but repeated burns caused by applying heated materials may have been responsible for tumor development. Penetration asphalts diluted with organic solvents (acetone or benzene) produced an average tumor incidence of 2-2.7% indicating that whole asphalts had little or no carcinogenic activity. Skin painting of oxidized asphalts diluted with acetone, benzene or toluene gave more variable results, from essentially non-carcinogenic [0 or 2% tumor incidence] to weak [10% tumor incidence] (Hueper and Payne, 1960; Emmett et al., 1981). In a single study with 45% tumor incidence in which asphalt was diluted in toluene (Simmer, 1965), severe skin irritancy induced by the toluene vehicle may have exacerbated the tumorigenic response. Skin effects from exposure of Swiss Albino mice to 8 different petroleum asphalts at concentrations of 25µl (10% in benzene), applied to the shaved backs twice a week for 81 weeks, included epidermal hyperplasia, inflammatory infiltration of the dermis, cutaneous ulceration and abscesses, and amyloidosis of the spleen and kidney. However only 6 of 218 mice (2.7%) exposed to any asphalt developed skin tumors (Wallcave et al., 1971; IARC, 1985). Vacuum residuum samples (API 81-13, API 81-14) diluted in toluene, were applied to the shaved backs of C3H/HeJ male mice (100/group) at an application volume of 50µl, twice a week for approximately 130 weeks. After 12 months, 50 mice/group were terminated; no definitive systemic toxicity was observed although skin damage at the treatment site was evident (API, 1986). At the end of 130 weeks, There were tumors in 5 mice treated with API 81-13; the tumors had a mean latency period of 113 weeks, and treatment with API 81-14 resultedin tumors in 2 mice with a mean latency period of 120 weeks compared to a toluene control of 4 mice with tumors and a mean latency of 111 weeks. Neither vacuum residuum sample was carcinogenic in this assay (API, 1989a), nor did either sample act as a tumor initiator or promoter in a short-term initiation-promotion assay in CD-1 mice (API, 1989b). A two-year skin painting study of an AC-20 paving asphalt diluted in USP mineral oil and administered twice a week at concentrations of 37.5ml per application for 24 months, also did not show tumor induction in dermally treated mice (McGowan et al., 1992). Overall, undiluted asphalts of all types are not carcinogenic by dermal exposure, but dilution of asphalts with organic solvents may not produce tumors or may show evidence of weak tumorigenic activity over a long duration of treatment.

Asphalt Fumes

Fume condensates generated in the laboratory from Type I and Type III roofing asphalt at 232^{0}C and 316^{0}C (450^{0}F and 601^{0}F) were applied biweekly to the shaved backs of male CD-1 (nonpigmented) and C3H/HeJ (pigmented) mice (50mice/group) for 78 weeks; one half of each group was exposed to simulated sunlight (Niemeier et al, 1988). Asphalt samples were heated over time intervals of 4 - 16.5 hours, in some cases repeatedly, to produce sufficient fume for testing. Generation conditions also included continuous agitation (200rpm) and heating under vacuum (10L/m), conditions which are not found when asphalt fumes are produced in the field. Tumors were induced by fume condensates from both types of asphalt; C3H mice demonstrated a greater response than CD-1 mice with a higher tumor incidence and shorter time-to-tumor latency period than CD-1 mice. The tumorigenic response of both types of asphalt was greater from fumes

generated at 316^{0}C (601^{0}F) compared to fumes generated at 232^{0}C (450^{0}F). Mean latency increased with simulated sunlight, which generally inhibited tumorigenic response. Sivak et al. (1989, 1997) heated Type III roofing asphalt from the same lot as Niemeier et al (1988) to 316^{0}C (601^{0}F), generated fumes, separated them into fractions A-E by HPLC, and analyzed fractions by GC/MS [Mutagenicity results for these fractions are discussed in the *in vitro* genetic toxicity section 7.1.3.1]. Raw roofing asphalt, neat asphalt fumes, asphalt residue after fumes were generated, reconstituted fumes and fume fractions individually or in various combinations were tested for carcinogenic and tumor-promoting activity in C3H/HeJ or Sencar mice (30 mice/group). Test material was applied twice a week for up to 104 weeks. Tumor-promotion was evaluated by a single initiating treatment with B(a)P followed by individual application of fraction A (alkanes, alkylated benzenes, alkylated naphthalenes), D (alkylated phenols, alkylated ketones) or E (C6-C22 alkylated ketones, alkylated naphthols, and phenols), considered by the investigators as the fractions most likely to exhibit promoting or cocarcinogenic activity. Results indicated that raw roofing asphalt was only weakly carcinogenic (3/30 tumor bearing C3H mice), asphalt residue after fume generation was not carcinogenic, and neat asphalt fumes were dermally carcinogenic (20/30 C3H mice). Only fractions B and C which contained PAHs, S-PAC and O-PAC induced carcinomas (10/30 mice, 17/30 mice, respectively; other fractions (A, D, E) were not carcinogenic and did not act as tumor promoters or co-carcinogens in Sencar mice. Only combinations of fractions containing B or C induced carcinomas.

Although these skin-painting studies indicate that asphalt fumes generated at high temperatures under laboratory conditions produce skin tumors in mice, chemical characterization of field-generated and laboratory-generated asphalt fumes have demonstrated that the fumes are compositionally different (McCarthy et al., 1999). In the Niemeier et al, (1988) studies described above, asphalts were heated to higher temperatures under vacuum and with continuous agitation for significantly longer periods of time in order to generate sufficient fumes for testing. These extreme methods produced a fume in which the yield of volatile “light end” components was much greater than found under field conditions. Thermal cracking, volatilization of constituents not released from asphalts under workplace conditions and other chemical reactions inconsistent with “real world” usage, make the results of these studies difficult to extrapolate to workplace hazard to man.

Fluorescence spectroscopy has also been used as a predictor of carcinogenicity for asphalt fumes. A method was developed that shows a high correlation between fluorescence emission intensity and carcinogenicity for 36 laboratory generated fume fractions, as measured in a mouse skin-painting bioassay (Osborn et al., 2001). Significantly, this method was then used to estimate the carcinogenic potential of U.S. paving worker samples. Emission levels, and therefore predicted carcinogenicity for these worker samples were at least 17-fold below the value that corresponds to a minimal carcinogenic effect, indicating that the cancer-causing components identified in the Niemeier et al, (1988) rodent studies are not present at measureable levels in asphalt fumes to which workers could be exposed (Kriech et al., 2002).

TABLE 4 Asphalt carcinogenicity studies

MATERIAL TESTED	TREATMENT	DURATION	RESULTS	REFERENCE
Skin Application of Whole Asphalts				
Penetration asphalts				

Steam refined (1 sample)	Undiluted (heated)	21 months	5/63 mice with skin tumors 21/63 mice survived study	Simmers (1965)
Road bitumen (4 samples)	Diluted with acetone (concentration unspecified) Application twice/week	2 years	0/100, 2/50, 1/50 & 0/50 mice with skin tumors	Hueper & Payne (1960)
Penetration bitumens (4 samples)	40% in benzene Application once/week	19 months	9/52, 4/47, 2/50 &2/50 mice with skin tumors	Kireeva (1968)
Penetration bitumen (8 samples)	10% in benzene Application twice/week	>81 weeks	Highest incidence 7% Lowest incidence 0% Overall incidence 2.7%	Walcave et al (1971)
Penetration bitumen (1 sample)	30% in mineral oil Application twice/week	24 months	0/50 mice	McGowan et al (1992)
<u>Hard Asphalts</u>				
Bitumen paint (1 sample)	60% bitumen in mineral spirit Application once/week	30 weeks	1/40 mice with skin tumor	Robinson et al (1984)
<u>Oxidized bitumens</u>				
Air blown bitumen (1 Sample)	90% in toluene Application three times/week	2 Years	9/20 mice with skin tumors	Simmers (1965)
Roofing bitumen (1 Sample)	Diluted in acetone, concentration unspecified Application twice/week	2 Years	1/50 mice with skin tumors	Hueper & Payne (1960)
Roofing bitumen (1 sample)	50% in toluene Application twice/week	80 weeks	0/50 mice with skin tumors	Emmet et al (1981)
Roofing bitumen (1 sample)	50% in acetone/cyclohexane Application twice/week	2 Years	3/30 mice with skin tumors	Sivak et al (1989)
<u>Vacuum residuum</u>				
2 samples API 81-13 & 81-14	Diluted in toluene 50µl twice/week	130 weeks	5/50 & 2/50 mice with skin tumors Mean latency 113 & 120 wks	API (1989a)
Inhalation Carcinogenicity Studies				
Oxidized bitumen (1 sample)	Fumes generated at 250-275°F Exposure 5 hr/day, 4 days/week 65 Bethesda strain rats 13 Guinea pigs used	2 Years	No lung tumors, but extensive fibrosing pneumonitis was observed in rats	Hueper & Payne (1960)
Mixture of 6 penetration grades and oxidized bitumens	20 C57 mice exposed 30 mins/day, five days/week Aerosol generated at 250°F	17 months	1 animal with lung adenoma	Simmers (1964)
Mixture of 6 penetration grades and oxidized bitumens	30 C57 mice exposed 6-7½hrs/dayfive days/week Smoke generated at 250°F	21 months	Bronchitis, loss of bronchial coilia, epithelial atrophy, necrosis, pneumonitis	Simmers (1964)

			No lung tumors observed	
Skin Application of Condensed Fumes				
Type I & Type III asphalt	Fumes generated at 450 & 601°F Application twice/week as 50% solution in cyclohexane/acetone. Some animals also exposed to UV light CD 1 and C3H mice used	Up to 72 weeks	C3H more sensitive than CD-1. Greater tumor response from fume generated at the higher temperature.	Niemeier et al (1988)
Type III asphalt	Fumes generated same method as by Niemeier but at 601°F only C3H and Sencar mice used Sample applied twice weekly	104 weeks	C3H mouse 20/30 mice with tumors Sencar : 14/30 mice with tumors	Sivak et al (1989, 1997)

CONCAWE, 1992

Conclusions: Undiluted asphalts of all types are not carcinogenic by dermal exposure and asphalts diluted in organic solvents are either non-carcinogenic or may exhibit weak dermal tumorigenic activity over a long duration of treatment. Skin-painting studies do indicate that asphalt fumes generated at high temperature under laboratory conditions produce skin tumors in mice. However, the analytical comparisons of field- and these laboratory-generated asphalt fumes indicate that they are compositionally dissimilar (McCarthy et al., 1999). The studies (Niemeier et al., 1988; Sivak et al., 1989, 1997) in which asphalts were heated to higher than recommended temperatures (232^0 and 316^0 C) with continuous agitation (200rpm) and under vacuum (10L/m) in order to produce sufficient fumes for testing, enhanced the production of atypical components. Thermal cracking and volatilization of constituents not released from asphalts under workplace conditions and other chemical reactions inconsistent with "real world" usage, make the results of those studies unrepresentative of the workplace hazard to man. In studies of more representative asphalt fumes, nose-only inhalation exposure of rats up to 172.5 mg/m^3 for 2 years to a partially oxidized bitumen fume condensate headspace of hot storage tank containing semi-blown paving bitumen (50/70 pen) did not result in tumors in any organ system, demonstrating that "real world" asphalt fumes alone are unlikely to induce systemic cancer in humans

8. HUMAN EXPOSURE SUMMARY

Humans are can be exposed to asphalt via the both the inhalation and dermal route of exposure, however, inhalation is considered to be the primary route of exposure. Occupational exposure to hot asphalt can lead to thermal burns; however, personal protective equipment normally prevents most skin contact. When asphalt is cold it becomes, solid, or semi-solid, and there is little personal exposure unless dust particles are generated, e.g., during removal of old materials containing asphalt (AI/Eurobitume, 2008). When asphalts are heated to facilitate paving or roofing applications, small quantities of the lighter, more volatile hydrocarbon vapors and gases and some inorganic gases (e.g., hydrogen sulfide) are emitted. As these components cool, they condense forming small droplets of liquid (fume), some of which have an effective diameter of less than 12.5 microns and are considered respirable (AI, 1990b; Brandt et al., 1985). At paving and roofing

worksites, the size distribution and the partitioning between gas, vapor and aerosol phase is strongly dependent on environmental conditions (AI/Eurobitume, 2008). Numerous sampling and analytical methods have been and continue to be employed in characterizing workplace exposure to asphalt fume. Exposure monitoring methods usually include measurements for total particulate matter (TPM), benzene soluble matter (BSM) and polycyclic aromatic hydrocarbons (PACs). One major cross sectional exposure assessment study conducted in the US showed that exposure to asphalt fume was below the current regulatory standards at that time (Hicks, 1995; Gamble et al, 1999). More recently, two excellent reviews summarized occupational exposure in the roofing and paving industry (AI/Eurobitume 2008; ARMA/BWA/NRCA/RCMA, 2008)

There are currently no specific OSHA standards for asphalt fumes. However, exposures to various chemical components of asphalt fumes are addressed in specific standards for the general and construction industries, such as personal protective equipment (PPE). OSHA standards, preambles to final rules (background to final rules), standard interpretations (official letters of interpretation of the standards), and compliance examples related to asphalt fumes can be found at http://www.osha.gov/SLTC/asphaltfumes/standards.html (OSHA 2009).

ACGIH® has a recommended TWA® (time weighted average) for Asphalt fume as benzene-soluble aerosol of 0.5 mg/m^3.

9. CATEGORY ANALYSIS CONCLUSIONS

The Asphalt Category comprises a single group of heavy residual streams derived from the high temperature vacuum distillation of petroleum. These complex substances typically boil above 450^{0}C (842^{0}F) [range of 400-550^{0}C (752-1021^{0}F)], have high molecular weights (500 - 5000), and high viscosity (300-500 cSt @ 100-135°C) in order to meet the use specifications in commercial asphalt formulations. Two category members, asphalt and oxidized asphalt represent >99% of all asphalt material end-uses such as asphalt paving (84%) and asphalt roofing (15%) applications. Less than 1% is used for other purposes such as waterproofing, damp proofing, insulation and paints (AI, 1990a)

The uses of asphalt create a dichotomous hazard profile between the ambient-temperature substances and the fumes generated from heated products. Potential hazards and environmental fates of the ambient-temperature substances are defined by the refining step of vacuum distillation. Evaluation of their common physical-chemical properties is sufficient to satisfy HPV requirements for all substances in this category. Toxic potential and environmental fate of the fumes generated from heated in-use products is directly related to the temperature of fume generation. Increasing temperatures dramatically increase the quantity, and also changes the physical-chemical properties of the fume. High temperature generation can also increase the PAH content of the fume. A sample that mimics fume observed in realistic high temperature field asphalt application (e.g., roofing) has been used to “bound” the composition of the fume from all members of the asphalt category for human health effects testing. The study endpoint measured data, and read-across values for untested category members are summarized in Appendix D. Matrix of Asphalt Category Data. Robust summaries are found in Appendix E, a separate document.

The physical-chemical characteristics of the members of the Asphalt Category show that these substances are solid to semi-solid viscoelastic substances with extremely high boiling

temperatures (>450 °C). They have negligible vapor pressures, partition coefficients estimated to be typically >10, and are essentially insoluble in water.

At ambient temperatures the semi-solid to solid nature of substances in the Asphalt Category and negligible vapor pressures and water solubility's limit their distribution to air or to aquatic compartments. Asphalts will tend to remain within the terrestrial or aquatic compartment to which they were released. During the applications of asphalts, fumes may be generated when the material is heated, and these fumes may condense onto local surfaces as they cool. Any vapors that remain suspended have the potential to interact with tropospheric OH radicals, and in this manner indirectly photodegrade within a matter of hours to a few days. Although hydrocarbons can be utilized as an energy source by microorganisms, asphalts would not dissolve or disperse in a manner to augment microbial attack. Due to the bulk properties of asphalt, a release to the environment would not result in measureable biodegradation.

The constituent hydrocarbons making up asphalt and vacuum residuum are of such high molecular weight and low solubility that they would not be expected to cause acute or chronic toxicity to aquatic organisms. Supporting data from petroleum streams with similar hydrocarbon structures (lubricating base oils and aromatic extracts aromatic extracts of vacuum distillates produced during manufacture of lubricant base oils) demonstrate aquatic toxicity in the range of 1000mg/L for fish, invertebrates and algae.

Asphalts and asphalt fumes demonstrate low acute toxicity by oral (LD50 rats>5.0 g/kg), dermal (LD50 rabbits>2.0 g/kg) and inhalation (LC50>94.4 mg/m^3) routes of exposure. Asphalts cause slight dermal irritation and mild to moderate eye irritation and are not skin sensitizers. Effects in humans under field conditions include mild and transitory eye irritation, nasal and throat irritation with exposure to fumes and some skin irritation has been reported with exposure to heated asphalt or asphalts with co-exposure to diesel fuel, coal tar or fiberglass.

Nose-only inhalation exposure of rats to roofing or paving asphalt fume condensate over durations of 28 to 90 days respectively resulted in a similar range of LOAEL values of 149.17 to 297.3 mg/m^3 the highest concentrations tested and NOAELs of 28.17 to 30.0 mg/m^3. In dermal exposure to asphalt, effects were seen primarily at the site of application but there were no systemic effects. Asphalt and asphalt fume condensates, representative of worker exposure, do not induce systemic toxicity at tested doses/concentrations.

Genetic toxicity studies demonstrated positive *in vitro* results with asphalt fume condensates in bacteria and slight activity in mammalian cells with metabolic activation. Severity of effect correlated with the temperature under which fumes were generated. Whole asphalts are non-mutagenic or only weakly mutagenic with metabolic activation in bacteria. Vacuum residuum administered orally or asphalt fume condensate administered by inhalation to laboratory animals under realistic fume generation and exposure conditions did not induce cytogenetic damage [chromosomal or micronucleus]. DNA adducts and strand breaks have been reported in some systems in the absence of definitive cytogenetic damage. Human data are highly variable and confounded by co-exposure to coal tar or other biologically active materials. Overall asphalts and asphalt fumes are not clastogenic *in vivo.*

Exposure to oxidized roofing asphalt fume condensate does not induce adverse effects on reproductive or developmental parameters and demonstrates that asphalt fume condensate is not a reproductive toxicant.

Carcinogenicity studies with asphalts include mouse skin painting studies with whole bitumens of different grades or asphalt fume condensates and 2-year inhalation studies with asphalt fumes. Undiluted asphalts of any type are not carcinogenic by dermal exposure and dilution of asphalts with organic solvents may be non-carcinogenic or may exhibit weak dermal tumorigenic potential over a long duration of treatment. Skin-painting studies do indicate that asphalt fumes generated at high temperatures under laboratory conditions produce skin tumors in mice. However, high temperature and long duration of heating can produce fumes containing constituents not released from asphalts under workplace conditions and other chemical reactions inconsistent with “real world” usage. Two year exposure of rats by nose-only inhalation to a partially oxidized bitumen fume condensate from the headspace of hot storage tank containing semi-blown paving bitumen (50/70 pen) representative of workplace exposure did not result in tumors in any organ system.

This testing program demonstrates that asphalt and asphalt fumes have generally low toxicity profiles for human health endpoints. Environmental results show asphalts are insoluble, not biodegradable and would not be expected to cause acute or chronic toxicity in aquatic organisms.

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11. LIST OF APPREVIATIONS AND ACRONYMS

API – American Petroleum Institute
BOD – biological oxygen demand
Btu/lb – British thermal unit per pound
Btu/scf – British thermal unit per standard cubic feet
AUGC – area under the growth curve
CAS RN/CAS #/CAS No. - Chemical Abstract Service Registry Number
^{o}C – degrees Celsius
CONCAWE – Conservation of Clean Air and Water in Europe
d - day
DMSO – Dimethyl sulfoxide
EINECS – European Inventory of Existing Commercial Chemical Substances
EL_{50} – effective loading rate lethal to 50% of the test population
E_bL_{50} – effective loading rate that causes 50% reduction in algal cell biomass
E_rL_{50} – effective loading rate that causes 50% reduction in algal growth rate
EPA/US EPA – United States Environmental Protection Agency
g/cm^3 – grams per cubic centimeter
h - hour
HPV – High Production Volume
^{o}K – degrees Kelvin
kPa - kilopascal
LC_{50} – lethal concentration for 50% of the test population
LD_{50}– lethal dose level for 50% of the test population
LL_{50} – lethal loading rate for 50% of the test population
Loading Rate – total amount of test substance added to dilution water to prepare water accommodated fractions (WAFs) for ecotoxicity testing
LOAEL – lowest observable adverse effect level
mg/kg – milligrams per kilogram
mg/L – milligrams per liter
mg/m^3 – milligrams per cubic meter
mL - milliliter
mm - millimeter
nm - nanometer
NOAEL – no observable adverse effect level
NOEC – no observable effect concentration
NOELR – no observable effect loading rate
OECD – Organization for Economic Cooperation and Development
OPPTS – US EPA Office of Prevention, Pesticides and Toxic Substances
PAC - Polycyclic aromatic compound
PAH – polycyclic aromatic hydrocarbon
Pen – Penetration grade of asphalt, also PG
PNA – polynuclear aromatic
ppm – part per million
SIDS – Screening Information Data Set
US EPA – United States Environmental Protection Agency
UV - ultraviolet
WAF – water accommodated fraction
wt% - weight percent
μg - microgram
μg/L – microgram/liter
> greater than
< less than
= equal to

12. Glossary

NOTE: *The following are general terms used in this and other HPV documents. To the extent possible definitions were taken from relevant authoritative sources such as US EPA, OECD, ASTM and IUPAC.*

Bioavailability: The state of being capable of being absorbed and available to interact with the metabolic processes of an organism. Typically a function of chemical properties, physical state of the material to which an organism is exposed, and the ability of the individual organism to physiologically take up the chemical. Also, the term used for the fraction of the total chemical in the environmental that is available for uptake by organisms. **(AIHA 2000)**

Category Member: The individual chemical or substance entities that constitute a chemical category.

Category: A chemical category, for the purposes of the HPV Challenge Program, is a group of chemicals whose physicochemical and toxicological properties are likely to be similar or follow a regular pattern as a result of structural similarity. These structural similarities may create a predictable pattern in any or all of the following parameters: physicochemical properties, environmental fate and environmental effects, and/or human health effects. **(US EPA 2007)**

Dose: The amount of a substance available for interactions with metabolic processes or biologically significant receptors after crossing the outer boundary of an organism. The **potential dose** is the amount ingested, inhaled, or applied to the skin. The **applied dose** is the amount presented to an absorption barrier and available for absorption (although not necessarily having yet crossed the outer boundary of the organism). The **absorbed dose** is the amount crossing a specific absorption barrier (e.g., the exchange boundaries of the skin, lung, and digestive tract) through uptake processes. **Internal dose** is a more general term denoting the amount absorbed without respect to specific absorption barriers or exchange boundaries. The amount of the chemical available for interaction by a particular organ or cell is termed the delivered or **biologically effective dose** for that organ or cell **(US EPA 2002b).**

Dose-Response Relationship: The relationship between a quantified exposure (dose) and the proportion of subjects demonstrating specific biological changes in incidence or in degree of change (response) **(US EPA 2002b).**

Ecological Effects – all endpoints (OECD definitions)

> **Fish, Acute Toxicity Test:** In a four-day exposure, acute toxicity is defined by the LC_{50}, the concentration of test substance in water which kills 50% of the test population of fish. Test methodology is described in OECD Guideline 203, in OECD Guidelines for the Testing of Chemicals.
>
> ***Daphnia* sp., Acute Immobilization Test:** In a one or two-day exposure, acute toxicity is defined by the EC_{50}, the concentration of test substance in water which causes immobilization to 50% of the test population of invertebrates. Test methodology is described in OECD Guideline 202, Part 1, in OECD Guidelines for the Testing of Chemicals.

Alga, Growth Inhibition Test: In a three-day exposure, growth inhibition is defined by the EC_{50}, the concentration of test substance in growth medium which results in a 50% reduction in either alga cell growth or growth rate relative to a control group. Test methodology is described in OECD Guideline 201, in OECD Guidelines for the Testing of Chemicals.

Endpoint: In the context of the EPA High Production Volume Challenge Program, an endpoint is a physical-chemical, environmental fate, ecotoxicity, and human health attribute measurable by following an approved test methodology (e.g., OECD Guidelines for Testing of Chemicals). Melting point, biodegradation, fish acute toxicity, and genetic toxicity are examples of endpoints that are measured by an approved test method. **(US EPA 2002a)**

Environmental Fate Effects – all endpoints (OECD definitions)

Photodegradation: The photochemical transformation of a molecule into lower molecular weight fragments, usually in an oxidation process. This process may be measured by Draft OECD Guideline, "*Phototransformation of Chemicals in Water – Direct and Indirect Photolysis*". This process also may be estimated using a variety of computer models.

Stability in Water: This environmental fate endpoint is achieved by measuring the hydrolysis of the test substance. Hydrolysis is defined as a reaction of a chemical RX with water, with the net exchange of the group X with OH at the reaction center. Test methodology for hydrolysis is described in OECD Guideline 111, in OECD Guidelines for the Testing of Chemicals.

Transport Between Environmental Compartments: This endpoint describes the distribution of a chemical between environmental compartments using fugacity-based computer models. The results of the model algorithms provide an estimate of the amount of the chemical within a specific compartment. The environmental compartments included in many models are air, water, soil, sediment, suspended sediment, and aquatic biota.

Biodegradation: Breakdown of a substance catalyzed by enzymes *in vitro* or *in vivo*. As an endpoint in EPA's HPV program, biodegradation is measured by one of six methodologies described in OECD Guidelines 301A-F, in OECD Guidelines for the Testing of Chemicals.

Exposure: Contact made between a chemical, physical, or biological agent and the outer boundary of an organism. Exposure is quantified as the amount of an agent available at the exchange boundaries of the organism (e.g., skin, lungs, gut). **(US EPA 2002b).**

Feedstock: A refinery product that is used as the raw material for another process; the term is also generally applied to raw materials used in other industrial processes. **(Speight, 2007).**

Female Mating Index: Number of females with confirmed mating (sperm and/or vaginal plug)/number of females placed with males. (**US EPA 1996).**

Hazard Assessment: The process of determining whether exposure to an agent can cause an increase in the incidence of a particular adverse health effect (e.g., cancer, birth defect) and whether the adverse health effect is likely to occur in humans **(US EPA 2002b)**.

Hazard Characterization: A description of the potential adverse health effects attributable to a specific environmental agent, the mechanisms by which agents exert their toxic effects, and the associated dose, route, duration, and timing of exposure **(US EPA 2002b).**

Hazard: A potential source of harm **(US EPA 2002b**).

Health Effects – all endpoints (OECD definitions, unless otherwise specified)

Acute Toxicity: The adverse effects occurring within a short time-frame of administration of a single dose of a substance, multiple doses given within 24 hours, or uninterrupted exposure over a period of 24 hours or less. Exposure may be via oral, dermal or inhalation routes as described in OECD Guidelines 401, 402, 403, and 420 in OECD Guidelines for the Testing of Chemicals.

Developmental Toxicity: Adverse effects on the developing organism that may result from exposure prior to conception (either parent), during prenatal development, or postnatally until the time of sexual maturation. The major manifestations of developmental toxicity include death of the developing organism, structural abnormality, altered growth, and functional deficiency. **(US NLM 2007)**

Genetic Toxicity *in vivo* (Chromosomal Aberrations): The assessment of the potential of a chemical to exert adverse effects through interaction with the genetic material of cells in the whole animal. Genotoxicity may be studies in the whole animal using methods described in OECD Guideline 475, in OECD Guidelines for the Testing of Chemicals.

Genetic Toxicity *in vitro* (Gene Mutations): The assessment of the potential of a chemical to exert adverse effects through interaction with the genetic material of cells in cultured mammalian cells. Genotoxicity may be studies in cultured cells using methods described in OECD Guideline 476, in OECD Guidelines for the Testing of Chemicals.

Repeated Dose Toxicity: The adverse effects occurring due to repeated doses that may not produce immediate toxic effects, but due to accumulation of the chemical in tissues or other mechanisms, produces delayed effects. Repeated dose toxicity may be studied following methods described in OECD Guidelines 407, 410, or 412 in OECD Guidelines for the Testing of Chemicals.

Reproductive Toxicity: The occurrence of biologically adverse effects on the reproductive systems of females or males that may result from exposure to environmental agents. The toxicity may be expressed as alterations to the female or male reproductive organs, the related endocrine system, or pregnancy outcomes. The manifestation of such toxicity may include, but not be limited to, adverse effects on onset of puberty, gamete production and transport, reproductive cycle normality, sexual behavior, fertility, gestation, parturition, lactation, developmental toxicity, premature reproductive senescence, or modifications in other functions that are dependent on the integrity of the reproductive systems. **(US EPA 1996)**

Lowest-Observed-Adverse-Effect Level (LOAEL): The lowest exposure level at which there are statistically or biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control group **(US EPA 2002b).**

Modified Ames Test now identified as **Optimized Ames Test:** Test designed to optimize exposure of insoluble complex petroleum mixtures to *Salmonella typhimurium* to evaluate mutagenicity [see ASTM Method E1687-95], involving extraction of the test material to concentrate condensed ring aromatic hydrocarbons (PAC), alteration of the rodent liver activating system to maximize metabolism [replacement of rat with hamster liver homogenate and six-fold increase in concentration] and testing in *Salmonella* strain TA98, the strain most sensitive to PAC.

Mutagenic Index: Mutagenic activity in the Optimized Ames test is reported as the Mutagenic Index [MI], the slope of the initial linear portion of the dose response curve [revertant/µL]. Oils with MI<1.0 are unlikely to be dermally carcinogenic; oils with MI>1.0<2.0 are marginal and MI>2.0 are likely dermal carcinogens. Oils producing MIs close to the values separating categories may be indiscernibly different in carcinogenicity assays from oils having Mis on the other side of that boundary.

No-Observed-Adverse-Effect Level (NOAEL): The highest exposure level at which there are no biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control group; some effects may be produced at this level, but they are not considered adverse or precursors to adverse effects **(US EPA 2002b)**.

Optimized Ames Test: see definition for Modified Ames Test above.

Petroleum (crude oil): A naturally occurring mixture of gaseous, liquid, and solid hydrocarbon compounds usually found trapped deep underground beneath impermeable cap rock and above a lower dome of sedimentary rock such as shale; most petroleum reservoirs occur in sedimentary rocks of marine, deltaic, or estuarine origin **(Speight 2007)**.

Read Across: Read-across can be regarded as using data available for some members of a category to estimate values (qualitatively or quantitatively) for category members for which no such data exist. **(OECD 2007)**

Systemic Effects or Systemic Toxicity: Toxic effects as a result of absorption and distribution of a toxicant to a site distant from its entry point **(US EPA 2002b)**.

Target Organ: The biological organ(s) most adversely affected by exposure to a chemical or physical agent **(US EPA 2002b).**

APPENDIX 1: ASPHALT HPV CATEGORY

Asphalt, CAS #8052-42-4.

A very complex combination of high molecular weight organic compounds containing a relatively high proportion of hydrocarbons have carbon numbers predominantly greater than C25 with high carbon-to-hydrogen ratios. It also contains small amounts of various metals such as nickel, iron, or vanadium. It is obtained as the non-volatile residue from distillation of crude oil or by separation as the raffinate from a residual oil in a deasphalting or decarbonization process.

Residues (petroleum), vacuum, CAS #64741-56-6.

A complex residuum from the vacuum distillation of the residuum from atmospheric distillation of a crude oil. It consists of hydrocarbon having carbon numbers predominantly greater than C34 and boiling above approximately 495^0C (923^0F).

Raffinates (petroleum), residual oil decarbonization, CAS #64742-07-0.

A complex combination of hydrocarbons obtained as the solvent insoluble fraction from C5-C7 solvent decarbonization of a residual oil. It consists predominantly of aromatic hydrocarbons having carbon numbers predominantly higher than C34 and boiling above approximately 495^0C (923^0F).

Petroleum Resins, CAS #64742-16-1.

A complex combination of organic compounds, predominantly hydrocarbons, obtained as a fraction of the extract of solvent extraction of residuum. It consists predominantly of high molecular weight compounds with high carbon-to-hydrogen ratios.

Residues (petroleum), hydrodesulfurized vacuum, CAS #64742-85-4.

A complex combination of hydrocarbons obtained by treating a vacuum residuum with hydrogen in the presence of a catalyst under conditions primarily to remove organic sulfur compounds. It consists of hydrocarbons having carbon numbers predominantly greater than C34 and boiling above approximately 495^0C (923^0F).

Asphalt, oxidized, CAS #64742-93-4.

A complex black solid obtained by blowing air through a heated residuum, or raffinate from a deasphalting process with or without a catalyst. The process is principally one of oxidative condensation which increases the molecular weight.

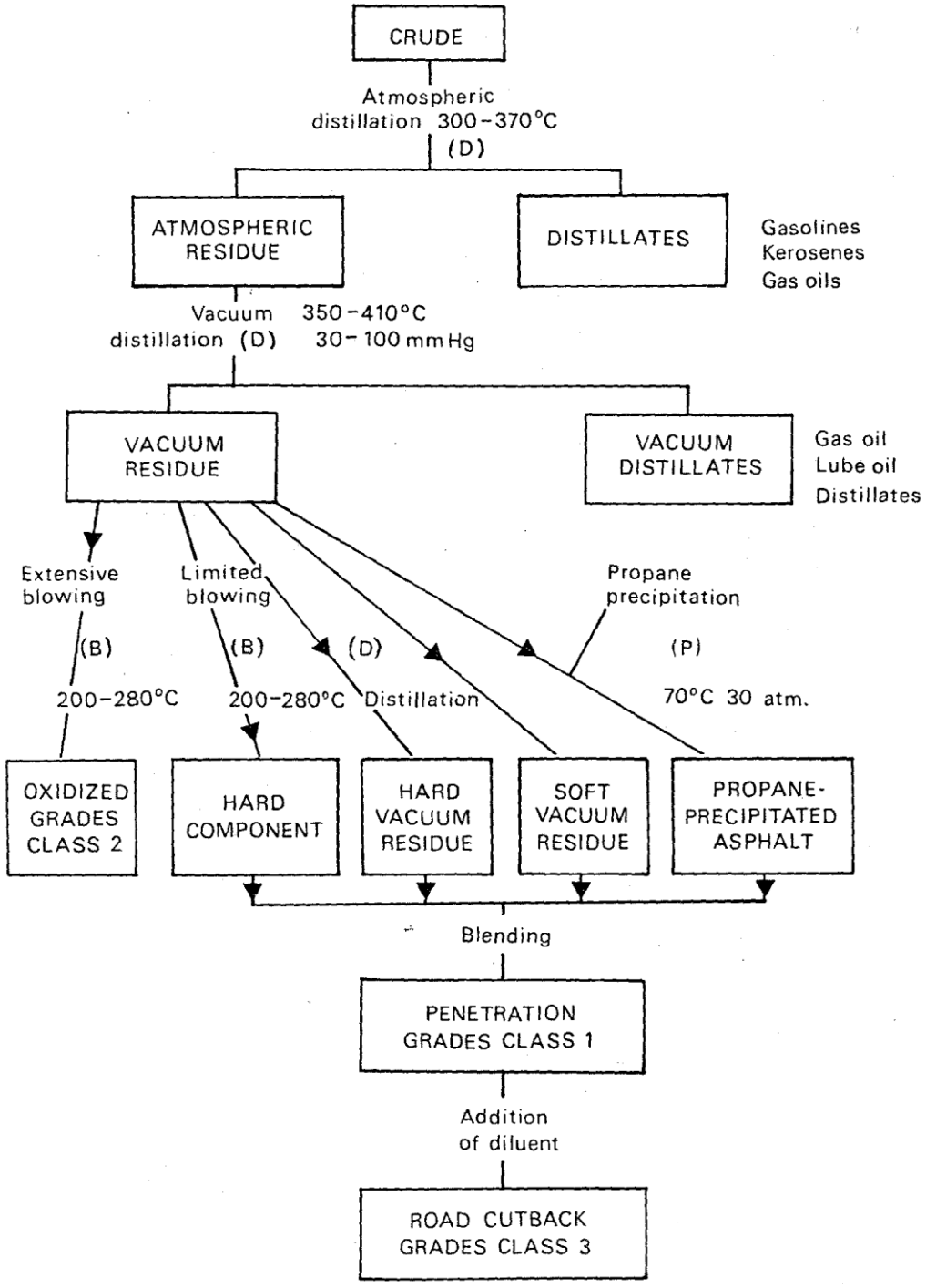
APPENDIX B: ASPHALT MANUFACTURE [CONCAWE, 1992; IARC, 1985]

Asphalts are produced from petroleum crude oils by low temperature non-destructive refining processes that remove most species boiling below 542^{0}C (1000^{0}F) and avoid high temperatures or other conditions that result in significant thermal cracking. (Figure A2-1).

- Atmospheric distillation **(D)** of crude oil at temperatures usually not exceeding 385^{0}C (725^{0}F) yields volatile fractions [e.g. gasoline, kerosene, gas oil] and heavier atmospheric residue with the consistency of fuel oil.
- Vacuum distillation **(D)** further refines the atmospheric residue to produce lubricating oil distillate fractions and a vacuum residuum. Distillation is performed at lower pressure and a temperature in the range of 380^{0}C (716^{0}F) to avoid thermal cracking. The vacuum residue from heavy crude oils may be sold as commercial asphalt, and the residue from lighter crude oils is feedstock for further processing.
- Air blowing **(B)** involves introducing air under pressure into asphalt feedstock, usually heated to 220-300^{0}C (428-572^{0}F) and sometimes in the presence of catalyst, to produce higher molecular weight compounds which give a harder, less temperature sensitive product, by oxidation and condensation polymerization. The asphaltene content is increased while the cyclic aromatic content decreases. Moderate blowing is used to obtain hard road asphalt or viscosity grade asphalts from vacuum residues. Severe treatment produces oxidized asphalts suitable for a wide range of building and industrial applications.
- Solvent precipitation **(P)** or deasphalting is employed to remove asphaltic compounds from certain vacuum residues to leave valuable high viscosity base oils (bright stocks) for lubricants. Residuum is dissolved in liquid propane or a propane/butane mixture, and the aliphatic fraction is precipitated and drawn off. Solvent precipitated asphalts have a higher content of asphaltenes than the vacuum residuum from which they are produced but a lower content of saturates than would be obtained by distillation of the vacuum residue.
- Thermal conversion reduces large paraffinic molecules to smaller ones and, to a lesser degree, a condensation occurs increasing asphaltenes and resins. The process is used primarily with residues from lighter crude oils to modify the ratios of paraffins, resins and asphaltenes. During this cracking process, some polycyclic aromatic compounds (PAC) are formed. The thermal residue is then distilled in a vacuum unit to remove volatiles including PAC and the remaining residue is used as a component of blended asphalt.

Ancillary Processes
Products from all these processes can be combined to meet performance specifications. Additional blending, cutting-back [mixing with volatile petroleum diluents], or fluxing [addition of high boiling (>350^{0}C) heavy distillates or industrial process oils) can provide further product flexibility.

Figure A2-1: Main Processing methods in the manufacture of asphalts



VR, vacuum residue; PPA, propane-precipitated asphalt

from IARC, 1985

APPENDIX C: Commercial Uses of Asphalts [AI, 1990b, 2003; NIOSH, 2000]

Roofing:

1- Roofing asphalts are graded as Type I, II, III, or IV in increasing order of hardness. These products are commonly liquefied by heating and applied directly during construction. Mopping grade roofing asphalts are used as an interply adhesive or top coating for asphalt saturated felts on built-up roofs. To insure proper performance and longevity, and to avoid product degradation due to overheating, roofing asphalts are typically heated to between 450-525^{0}F on the job site and applied at lower temperatures of 330-445^{0}F at the point of mopping. The slope of the roof decides the grade of asphalt used; as the slope increases so does the hardness and grade of asphalt [Table C-1].

Table C-1. Grades and characteristics of roofing asphalts

Type	Characteristics	Typical Application Temp.
I	Low softening point; soft roofing or dead level asphalt for inclines up to 0.5 inch/ft	330-355^{0}F (166-179^{0}C)
II	For inclines of 0.5-1.5 inches/ft	365-390^{0}F (185-199^{0}C)
III	For inclines of 1-3 inches/ft	395-420^{0}F (202-216^{0}C)
IV	High softening point, hard roofing asphalt for inclines from 2-6 inches/ft	430-445^{0}F (221-229^{0}C)

Asphalt Institute, 1990b

Roofing asphalts are usually manufactured by blowing air through a heated residuum [usually a vacuum residuum] with or without a catalyst.

2- Asphalt shingles (saturated felts, coated fabrics, coated glass fibers)
The saturant or coating asphalt is produced by blowing air through heated residuum, which is mixed with mineral filler at the roofing plant and applied to an organic or inorganic matting to produce granule surfaced shingles, smooth surface shingles, smooth roll ply sheets or granule surfaced roll sheets.

3- Modified bitumen roll roofing materials
In the roofing plant, non-blown, viscosity graded asphalt cement is heated and mixed with fillers and a polymer or copolymer which is then impregnated onto an inorganic reinforcing matting and formed as a granule surfaced or smooth surfaced roll. This material is normally installed on a roof as a mutilayer membrane system.

Paving:

There are three types of asphalt products used in the building of roads and other paved surfaces.

1- Hot Mixed Asphalt [HMA] is a blend of asphalt paving cement and mineral aggregates. Asphalt paving cement is the straight reduced or vacuum processed asphalt used mainly as a binder (4-10%) of hot mixed asphalts to hold the aggregate together. HMA materials comprise 85% of

all paving products and are the most important commercially and in terms of number of workers exposed.

2- Cutback asphalts are a mixture of asphalt with volatile petroleum diluents such as white spirits, kerosene or gas oil to render them more fluid for ease of handling and application. When the diluent evaporates, the initial properties of the asphalt are recovered. These products are used in spray applications as surface treatments and are handled at temperatures ranging from ambient to 300^0F. However, air quality concerns have restricted their use.

3- Asphalt emulsions are fine dispersions of heated asphalt [base asphalt used in HMA applications] in water with an emulsifying agent. They are classified as cationic [electro-positively charged micelles containing asphalt molecules], or anionic [electro-negatively charged micelles containing asphalt molecules] depending on the emulsifying agent, and are graded according to chemical setting time. They can be applied as sprays or in cold mix applications for seal coating, maintenance and repair.

4- Mastic asphalt is a mixture of asphalt and fine mineral material in proportions so that it may be poured hot in place then compacted by hand troweling to a smooth surface for flooring, roofing and paving. It is not commonly used in the US.

Asphalt based Paints:
This product is specialized cutback asphalt that can contain small amounts of other materials such as lampblack, aluminum flakes or mineral pigments. These paints are used as protective coatings in waterproofing operations and similar applications.

<u>Specification Tests</u>

Viscosity Test: Resistance to flow is measured at temperatures of 60^0C (140^0F), the maximum temperature of set asphalt pavement surfaces in US, and 135^0C (275^0F), the maximum mixing and lay-down temperature for hot asphalt pavements, using capillary or orifice-type viscometers.

Penetration Test: Indentation of an asphalt sample in tenths of a millimeter at 25^0C is measured using a specified needle with a loading of 100g. Penetration grade is identified as pen or PG with the appropriate number value.

Softening Point test: Temperature is measured in ^{0}C at which asphalt, in the form of a disc under given loading conditions, softens and extends a fixed length.

<u>Asphalt Workers</u>

Approximately 3600 hot mix asphalt facilities and 7000 paving contractors employ nearly 300,000 workers in the US (data from Asphalt Paving Environmental Council, 1999 in NIOSH, 2000). Approximately 50,000 on-roof workers are exposed to asphalt fumes during, on average, 40% of their working hours, and 1500 to 2000 employees are exposed to asphalt fumes in approximately 100 roofing manufacturing plants (data from Asphalt Roofing Environmental Council, 1999 in NIOSH, 2000