



## ADDENDUM TO THE TOXICOLOGICAL PROFILE FOR CREOSOTE

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## CONTENTS

Background Statement .....	1
3. HEALTH EFFECTS .....	2
3.2 DISCUSSION OF HEALTH EFFECTS BY ROUTE OF EXPOSURE .....	2
3.2.1 Inhalation Exposure .....	2
3.2.2 Oral Exposure .....	4
3.2.3 Dermal Exposure .....	4
3.3 GENOTOXICITY .....	6
3.5 MECHANISMS OF ACTION .....	6
3.5.2 Mechanisms of Toxicity .....	6
3.8.1 Biomarkers Used to Identify or Quantify Exposure to Creosote .....	6
4. CHEMICAL AND PHYSICAL INFORMATION .....	7
5. PRODUCTION, IMPORT/EXPORT, USE, AND DISPOSAL .....	7
6. POTENTIAL FOR HUMAN EXPOSURE .....	7
6.3 ENVIRONMENTAL FATE .....	7
6.5 GENERAL POPULATION AND OCCUPATIONAL EXPOSURE .....	8
7. ANALYTICAL METHODS .....	9
7.2 ENVIRONMENTAL SAMPLES .....	9
8. REGULATIONS AND ADVISORIES .....	10
9. REFERENCES .....	10

**ADDENDUM FOR CREOSOTE**  
**Supplement to the 2002 Toxicological Profile for Creosote**

**Background Statement**

*This addendum to the Toxicological Profile for Creosote supplements the profile that was released in 2002.*

*Toxicological profiles are developed in response to the Superfund Amendments and Reauthorization Act (SARA) of 1986, which amended the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA or Superfund). CERCLA mandates that the Administrator of ATSDR prepare toxicological profiles on substances on the CERCLA Priority List of Hazardous Substances and that the profiles be revised “no less often than once every three years”. CERCLA further states that the Administrator will “establish and maintain inventory of literature, research, and studies on the health effects of toxic substances” [Title 42, Chapter 103, Subchapter I, § 9604 (i)(1)(B)].*

*The purpose of this addendum is to provide to the public and other federal, state, and local agencies a non-peer reviewed supplement of the scientific data that were published in the open peer-reviewed literature since the release of the profile in 2002.*

*Chapter numbers in this addendum coincide with the [Toxicological Profile for Creosote \(2002\)](#). This document should be used in conjunction with the profile. It does not replace it.*

### 3. HEALTH EFFECTS

#### 3.2 DISCUSSION OF HEALTH EFFECTS BY ROUTE OF EXPOSURE

##### 3.2.1 Inhalation Exposure

###### 3.2.1.1 Death

*Coal tar products.* Mortality from obstructive lung diseases in asphalt workers was reported to be associated with the estimated cumulative and average exposures to polycyclic aromatic hydrocarbons (PAHs) and coal tar, but confounding variables and bias could not be ruled out for the observed association (Burstyn et al., 2003).

In a 38-year follow-up of 332 male workers who were exposed to coal tar and coal tar pitch volatiles in a man-made graphite electrode factory for at least 5 years, the standard mortality ratio (SMR) for lung cancer significantly increased in comparison to the general population (SMR 2.62) and the local population (SMR 2.35). Even though smoking habits had been taken into account, the SMR for lung cancer was still high. The SMR for lymphatic and haematopoietic cancers was also significantly increased (SMR 3.46). However, the author cautioned about the limitations of the study, such as the small study population and insufficient information on exposure (Mori 2002).

###### 3.2.1.2 Systemic Effects

###### Renal Effects

*Coal Tar Products.* Advanced renal failure (chronic tubulo-interstitial nephritis) was reported in a 56-year old aromatherapist following chronic coal tar creosote vapor inhalation (Hiemstra et al., 2007).

###### 3.2.1.4 Neurological Effects

Long-term residents near a wood treatment plant who had low-level environmental exposure to wood processing waste chemicals had significantly more adverse health effects than unexposed

controls matched for gender and age; these health effects included cancer as well as respiratory, skin and neurological problems (Dahlgren et al., 2003). Their prevalence of mucous membrane irritation, skin and self-reported neurological symptoms such as irritability, light-headedness, and extreme fatigue, and cancer was significantly greater. In a comparison of the exposed versus the unexposed, 10% of the exposed had cancer versus 2.08% of the unexposed; bronchitis, 17.8% versus 5.8%; and asthma by history, 40.5% versus 11%. The exposed had significantly more neurophysiologic abnormalities in reaction time, trail making, and visual field defects. The plant used creosote and pentachlorophenol. The residents' potential exposure pathways included air, soil, surface water, and possibly drinking water contaminated with wood processing waste, including chlorinated dioxins and furans (Dahlgren et al., 2007).

***Coal Tar Products.*** Seizure, ataxia, cognitive impairment, and marked generalized cerebral atrophy were reported in a 56-year old aromatherapist following chronic coal tar creosote vapor inhalation (Hiemstra et al., 2007).

### **3.2.1.7 Cancer**

***Coal Tar Products.*** In a retrospective cohort study of 2,179 workers from 11 wood-treating plants in the United States in areas where wood was treated with creosote-based preservatives between 1979–2001, there was an assessment of the association of exposure to creosote with an increase in mortality from either site-specific cancers or nonmalignant diseases. A nested case-control study of lung cancer and multiple myeloma was also conducted. Overall mortality for the entire cohort was lower than expected, compared to the U.S. national mortality rate. Almost 90% of the employees were hourly workers whose exposure potential was expected to be higher than the exposure of salaried employees. Among hourly employees, only multiple myeloma showed a significant increase. However, further detailed analysis by length of employment did not show any upward trend for multiple myeloma. No statistically significant increase in mortality for any non-malignant diseases was reported. In the case-control study, an increased risk of lung cancer was associated with tobacco consumption, but not with any job/exposure category. Case-control analyses of multiple myeloma did not show any association with employment at the plants or with exposure to creosote-based preservatives or to creosote-treated products. Thus, there was no evidence that employment at the 11 wood-treating plants or

exposure to creosote-based preservatives was associated with any significant increase in mortality from cancers or non-malignant diseases. However, the authors cautioned that some of the study results were based on small numbers (Wong and Harris 2005).

### **3.2.2 Oral Exposure**

#### **3.2.2.5 Neurological Effects**

Long-term residents near a wood treatment plant who had low-level environmental exposure to wood processing waste chemicals had significantly more adverse health effects than unexposed controls matched for gender and age; the adverse health effects included cancer and respiratory, skin, and neurological problems (Dahlgren et al., 2003). The prevalence of mucous membrane irritation, skin and self-reported neurological symptoms such as irritability, light-headedness, and extreme fatigue, and cancer was significantly greater among exposed residents. The comparison of exposed versus unexposed for cancer was 10.0%, versus 2.08%; bronchitis, 17.8% versus 5.8%; and asthma by history, 40.5% versus 11%. There were significantly more neurophysiologic abnormalities in reaction time, trail making, and visual field defects among exposed residents. The plant used creosote and pentachlorophenol. The residents' potential exposure pathways included air, soil, surface water, and possibly drinking water contaminated with wood processing waste, including chlorinated dioxins and furans (Dahlgren et al., 2007).

**Wood Creosote.** Altered taste and somnolence were the most common side-effects in people taking 180 and 225 mg of Seirogen (Kuge et al., 2003a; Kuge et al., 2003). Wood creosote is the principal active ingredient of Seirogen, which is a herbal anti-diarrheal and anti-spasmodic medication used in Asia. Single oral doses of wood creosote up to 225 mg were found to be safe and well tolerated in healthy men and women. Oral doses of wood creosote consisting of 45–225 mg every two hours for up to five doses were reported to be safe and well tolerated in 45 health subjects.

### **3.2.3 Dermal Exposure**

#### **3.2.3.3 Immunological and Lymphoreticular Effects**

**Coal tar products.** Immunological modulation of pro-inflammatory cytokines (IL-8) and adhesion molecules (sE-selectin, sP-selctin, sICAM1) was reported in patients with psoriasis treated with Goeckerman's therapy (GT), which combined dermal application of crude coal tar (containing polycyclic aromatic hydrocarbons—PAHs) and exposure to UV radiation. GT also caused significantly decreased levels of serum IgE, IgM, alpha(2)macroglobulin, transferrin, and beta(2)-microglobulin in treated psoriasis patients; however, only the decreased level of alpha(2)-macroglobulin was found to correlate with exposure to PAHs (Borsk et al., 2006a;Borsk et al., 2006b).

#### **3.2.3.4 Neurological Effects**

Long-term residents near a wood treatment plant who had low-level environmental exposure to wood processing waste chemicals had significantly more adverse health effects than unexposed controls matched for gender and age; the adverse health effects included cancer and respiratory, skin, and self-reported neurological symptoms such as irritability, light-headedness, and extreme fatigue (Dahlgren et al., 2003). The prevalence of mucous membrane irritation, skin and neurological symptoms, and cancer was significantly greater among exposed residents; 10% of exposed residents had cancer, versus 2.08% of the unexposed; bronchitis, 17.8% versus 5.8%; and asthma by history, 40.5% versus 11%. There were significantly more neurophysiologic abnormalities in reaction time, trail making and visual field defects among exposed residents. The plant used creosote and pentachlorophenol. The residents' potential exposure pathways included air, soil, surface water, and possibly drinking water contaminated with wood processing waste, including chlorinated dioxins and furans (Dahlgren et al., 2007).

#### **3.2.3.7 Cancer**

**Coal Tar Products.** Squamous cell carcinoma of the skin in a non-sun-exposed skin area in a railroad worker was reported to result from 30 years of coal tar creosote-soaked clothing (Carlsten et al., 2005).

### 3.3 GENOTOXICITY

**Coal Tar Products.** Chromosomal aberrations of peripheral lymphocytes were found in patients with psoriasis after treatment with Goeckerman's therapy (GT), which includes dermal application of coal tar (polycyclic aromatic hydrocarbons—PAHs) and UV radiation. The levels of chromosomal aberrations correlated to exposure to PAHs (Borsk et al., 2006b). Significant increased urinary mutagenicity was found in samples in the middle and end of the GT regimen (Fiala et al., 2006).

A single painting of coal tar caused strong genotoxic effects in the mouse epidermis, as shown by induction of DNA strand breaks and DNA adducts in hairless mice and *lacZ* mutations in transgenic mice (Muta Mouse) (Thein et al., 2000).

### 3.5 MECHANISMS OF ACTION

#### 3.5.2 Mechanisms of Toxicity

Wood creosote may be of clinical value as an anti-diarrhea agent because it inhibits enterotoxin-induced intestinal fluid secretion by affecting Cl<sup>-</sup> secretion in intestinal epithelium. 4,5-Dimethylresorcinol, a component of wood creosote, was identified as the active constituent to inhibit rat intestinal Cl<sup>-</sup> secretion with a half-inhibitory concentration of 3.8 µg/mL (28 µmol/L). The inhibitory effect was suggested to be due to inhibition of Cl<sup>-</sup> channels (Ogata and Shibata 2004).

### 3.8 BIOMARKERS OF EXPOSURE AND EFFECT

#### 3.8.1 Biomarkers Used to Identify or Quantify Exposure to Creosote

**Coal Tar Products.** The measurement of urinary naphthalene metabolites  $\alpha$ - and  $\beta$ - naphthol by gas chromatography/mass spectroscopy (GC/MS) has been reported to be sufficiently sensitive to detect exposure to low levels of PAHs of persons living near a creosote impregnation plant. The exposure to pyrene was too low to reflect significant contribution of urinary 1-hydroxypyrene (1-OHP) from creosote impregnation plant emissions (Bouchard et al., 2001).



## 4. CHEMICAL AND PHYSICAL INFORMATION

No updated data.

## 5. PRODUCTION, IMPORT/EXPORT, USE, AND DISPOSAL

No updated data.

## 6. POTENTIAL FOR HUMAN EXPOSURE

### 6.3 ENVIRONMENTAL FATE

#### 6.3.2 Transformation and Degradation

##### 6.3.2.3 Sediment and Soil

High molecular weight PAHs in coal tar-contaminated sediments can be attenuated by *Mycobacteria* biodegradation. Fast-growing diverse *Mycobacterium* community was demonstrated in sediment samples from Chattanooga Creek Superfund site (Debruyn et al., 2007).

PAHs from soil contaminated with creosote can also be removed by biodegradation, using fungi. The white rot fungus *Pleurotus ostreatus* was reported to be a more efficient creosote-degrading organism than *Irpex lacteus* in a laboratory-scale study (Byss et al., 2008).

##### 6.3.2.4 Other Media

The white rot fungus *Pleurotus ostreatus* was reported to be effective in degradation of phenols and PAHs in creosote-treated wood (Galli et al., 2008).

## 6.5 GENERAL POPULATION AND OCCUPATIONAL EXPOSURE

Chemical contamination of wood processing waste (WPW) had been reported in residents and residential homes adjacent to a wood treatment plant that used creosote and pentachlorophenol (PCP) to treat wood for over 70 years (Dahlgreen et al., 2003a; Dahlgreen et al., 2007). For a period of time, the plant also burned treated wood products. Analysis of blood samples from 10 residents showed elevated octachlorodibenzo-*p*-dioxin and heptachlorodibenzo-*p*-dioxin, consistent with PCP as the source. Soil sediment and dust samples had higher than background levels of carcinogenic PAHs. The estimated air levels for benzo(a)pyrene and tetrachlorodibenzodioxin were also elevated.

Analysis of 319 breathing zone air samples and 31 general air samples indicated that exposures to coal tar pitch volatiles of workers at all jobs in 10 coke facilities surveyed in 1966 exceeded the threshold limit of 0.2 mg/m<sup>3</sup> TWA (Fannick et al., 1972).

Exposure to coal tar pitch volatiles (CTPV) has also been reported in aluminum smelter workers in Quebec (Lavoue et al., 2007). Exposures to CTPV were assessed by use of a job-exposure matrix (JEM) and estimated benzene-soluble material and benzo(a)pyrene (B[a]P) levels. The JEM incorporated job and time period, including 28,910 jobs, from 7 facilities from 1916 to 1999. Estimated exposures were 0.01–68.08 µg/m<sup>3</sup> B[a]P and 0.01–3.64 mg/m<sup>3</sup> BSM. The exposures were lowest before 1940 and after 1980.

Air samples and urinary 1-hydroxypyrene (1-OHP) in post-shift urine samples and next-day urine samples were analyzed for 36 creosote-exposed wood treatment plant workers (Borak et al., 2002). The results suggest that inhalation accounted for only a small portion of the absorbed dose; more than 90% of measured urinary 1-OHP came from dermal uptake, rather than inhalation. Determination of volatized PAHs in the breathing zone was more useful than the traditional analysis of benzene soluble fraction (BSF) of air samples for assessing creosote exposure.

Dermal exposure has also been reported to be an important route of occupational exposure to PAHs in asphalt roofing workers (McClellan et al., 2007). Dermal patch 1-OHP was measured to evaluate the effects of dermal exposure on total absorbed dose.

Coal tar has also been used therapeutically. Patients with atopic dermatitis and treated with topical coal tar preparations had increased urinary 1-OHP excretion rates (Veehuis et al., 2002). The urinary 1-OHP excretion rate was dependent on the amount of coal tar applied to the skin and the total body area treated, and less on the severity of the atopic dermatitis.

## 7. ANALYTICAL METHODS

### 7.2 ENVIRONMENTAL SAMPLES

Eriksson et al. (2001) reported direct analysis of hydrocarbons in PAH/creosote-contaminated soil by use of headspace solid phase microextraction (HS-SPME) and GC-MS. The concentrations using HS-SPME at 60° C correlated well with conventional ethyl acetate/hexane (20:80) liquid extraction for compounds containing up to 2 and 3 aromatic rings. The total concentrations for each compound using HS-SPME ranged from 2 to 25 µg/g soil.

PAHs and water-extractable phenols were measured in creosote and creosote-treated wood products made or procurable in Japan. PAHs were extracted with dichloromethane and analyzed by GC-MS (Ikarashi et al., 2005). Benz(a)anthracene was detected at 228–6,328 µg/g; benzo(b)fluoranthene, benzo(k)fluoranthene, and benzo(a)pyrene were detected at 67–3,541 µg/g. Concentrations of phenols in the range of 692–2,489 µg/g were detected in water extracts from creosotes.

Two-dimensional GC in tandem with quadropole MS provided enhanced separation of the complex components of the volatile fraction of creosote-treated wood, and it facilitated identification of isomer clusters such as alkylquinolines, alkylphenols, alkylbenzenes, and alkyl-naphthalenes (Mateus, et al., 2008).

## 8. REGULATIONS AND ADVISORIES

The U.S. Department of Health and Human Services has classified coal tar and coal tar pitches as known to be human carcinogens (NTP 2002).

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