

**PAHs (Cyclopenta[c,d]pyrene, Dibenz[a,h]anthracene, Dibenz[a,j]acridine, Dibenzo[a,l]pyrene, 1-Nitropyrene, 6-Nitrochrysene)  
[CAS No. 27208-37-3, 53-70-3, 224-42-0, 191-30-0, 5522-43-0, 7496-02-8]  
Occupational carcinogen: Group 2A**

The Japanese Society for Occupational Health (JSOH) has not judged the classification of polycyclic aromatic hydrocarbons (PAHs). The IARC judged the carcinogenicity of six PAHs, Cyclopenta[c,d]pyrene, Dibenz[a,h]anthracene, Dibenz[a,j]acridine, Dibenzo[a,l]pyrene, 1-Nitropyrene, and 6-Nitrochrysene, as Group 2A. This time, the JSOH reviewed the references related to Cyclopenta[c,d]pyrene<sup>1-3</sup>, Dibenz[a,h]anthracene<sup>1,4,5</sup>, Dibenz[a,j]acridine<sup>1,6,7</sup>, Dibenzo[a,l]pyrene<sup>8-10</sup>, 1-Nitropyrene<sup>11-13</sup>, and 6-Nitrochrysene<sup>11,14,15</sup>. There is no epidemiological study of workers exposed to each PAH independently. In experimental animals, there is sufficient evidence for carcinogenicity, e.g., lung adenoma for Cyclopenta[c,d]pyrene<sup>2</sup>, sarcoma for Dibenz[a,h]anthracene<sup>4</sup>, skin tumor for Dibenz[a,j]acridine<sup>6</sup>, skin tumor and lung adenoma for Dibenzo[a,l]pyrene<sup>9</sup>, lung tumor for 1-Nitropyrene<sup>12</sup>, and lung tumor for 6-Nitrochrysene<sup>14</sup>. Also, in the mechanistic aspect of experimental animal studies, there is sufficient evidence that the activated metabolites have genotoxicity, e.g., 3,4-dihydrocyclopenta (c,d) pyrene for Cyclopenta[c,d]pyrene<sup>3</sup>, 3,4-diol-1,2-epoxide for Dibenz[a,h]anthracene<sup>5</sup>, trans-3,4-dihydroxy-anti-1,2-epoxy-1,2,3,4-tetrahydroDBA (DBADE) for Dibenz[a,j]acridine<sup>7</sup>, both anti-and syn-11,12-dihydroxy-13,14-epoxy-11,12,13,14-tetrahydrodibenzo[a,l]pyrene (DB[a,l]PDE) for Dibenzo[a,l]pyrene<sup>10</sup>, 1-aminopyrene for 1-Nitropyrene<sup>13</sup>, and 1,2-dihydroxy-1,2-dihydro-6-aminochrysene for 6-Nitrochrysene<sup>15</sup>. Based on these findings, the JSOH judged these six PAHs as Group 2A.

Year of Proposal: 2016 (Group 2A)

### References

- 1) IARC. Monograph 92: Some Non-heterocyclic Polycyclic Aromatic Hydrocarbons and Some Related Exposures. Lyon: IARC, 2010: 425–426.
- 2) Busby WF Jr, Stevens EK, Kellenbach ER, et al. Dose-response relationships of the tumorigenicity of cyclopenta[cd]pyrene, benzo[a]pyrene and 6-nitrochrysene in a newborn mouse lung adenoma bioassay. *Carcinogenesis* 1988; 9 (5): 741–746.
- 3) Cavalieri E, Rogan E, Toth B, et al. Carcinogenicity of the environmental pollutants cyclopenteno-[cd]pyrene and cyclopentano[cd]pyrene in mouse skin. *Carcinogenesis* 1981; 2 (4): 277–281.
- 4) Flesher JW, Horn J, Lehner AF. Comparative carcinogenicity of picene and dibenz[a,h]anthracene in the rat. *Biochemical and Biophysical Research Communications* 2002; 290 (1): 275–279.
- 5) Buening MK, Levin W, Wood AW, et al. Tumorigenicity of the dihydrodiols of dibenzo(a,h)anthracene on mouse skin and in newborn mice. *Cancer Research* 1979; 39 (4): 1310–1314.
- 6) Warshawsky D, Barkley W, Miller ML, et al. Carcinogenicity of 7H-dibenzo[c,g]carbazole, dibenz[a,j]acridine and benzo[a]pyrene in mouse skin and liver following topical application. *Toxicology* 1994, 93 (2-3): 135–149.
- 7) Xue W, Schneider J, Mitchell K et al. trans-3,4-dihydroxy-anti-1,2-epoxy-1,2,3,4-tetrahydrodibenzo[a,j]acridine involvement in dibenz[a,j]acridine DNA adduct formation in mouse skin consistent with Ha-ras mutation patterns in tumors. *Chemical Research in Toxicology* 2001, 14 (7): 871–878.
- 8) IARC. Monograph 103: Bitumens and Bitumen Emissions, and Some N-and S-Heterocyclic Polycyclic Aromatic Hydrocarbons. Lyon: IARC, 2013: 241–246.
- 9) Higginbotham S, RamaKrishna NVS, Johansson SL, et al. Tumor-initiating activity and carcinogenicity of dibenzo[a,l]pyrene versus 7,12-dimethylbenzo[a]anthracene and benzo[a]pyrene at low doses in mouse skin. *Carcinogenesis* 1993; 14 (5): 875–878.
- 10) Prahalad AK, Ross JA, Nelson GB, et al. Dibenzo[a,l]pyrene-induced DNA adduction, tumorigenicity, and Ki-ras oncogene mutations in strain A/J mouse lung. *Carcinogenesis* 1997; 18 (10): 1955–1963.
- 11) IARC. Monograph 105: Diesel and Gasoline Engine Exhausts and Some Nitroarenes. Lyon: IARC, 2014: 621–688.
- 12) El-Bayoumy K, Hecht SS, Sackl T, et al. Tumorigenicity and metabolism of 1-nitropyrene in A/J mice. *Carcinogenesis* 1984; 5 (11): 1449–1452.
- 13) Malia SA, Vyas RR, Basu AK. Site-specific frame-shift mutagenesis by the 1-nitropyrene-DNA adduct N-(deoxyguanosin-8-y1)-1-aminopyrene located in the (CG) 3 sequence: effects of SOS, proofreading, and mismatch repair. *Biochemistry* 1996; 35 (14): 4568–4577.
- 14) Busby WF Jr, Garner RC, Chow FL, et al. 6-Nitrochrysene is a potent tumorigen in newborn mice. *Carcinogenesis* 1985; 6 (5): 801–803.
- 15) Boyiri T, Leszczynska J, Desai D, et al. Metabolism and DNA binding of the environmental pollutant 6-nitrochrysene in primary culture of human breast cells and in cultured MCF-10A, MCF-7 and MDA-MB-435s cell lines. *International Journal of Cancer* 2002; 100 (4): 395–400.