OCCUPATIONAL EXPOSURES DURING ALUMINIUM PRODUCTION

Aluminium production was considered by previous IARC Working Groups in 1983, 1987, and 2005 (IARC, 1984, 1987, 2010). Since 2005 new data have become available, which have been incorporated in this *Monograph*, and taken into consideration in the present evaluation.

1. Exposure Data

The aluminium-production industry as referred to in this *Monograph* involves processes such as the electrolytic reduction of alumina to aluminium, and the casting of aluminium into ingots. The mining of bauxite, production of alumina from bauxite, alloying and fabrication of sheet metal, wire, foil and other such products are not considered.

1.1 Natural occurrence

Aluminium, the third most abundant element in the earth's crust, occurs in nature in combination with silicon and oxygen (i.e. as aluminium silicate). When subject to tropical weathering, aluminium silicate may react to form aluminium hydroxide. Rock containing high concentrations of aluminium hydroxide is called bauxite. This rock is the usual starting material for the production of aluminium. Metallurgical-grade alumina (Al_2O_3) extracted from bauxite by the Bayer process is generally referred to as the ore (Sanders, 2002).

1.2 Manufacturing processes

The electrolytic process by which aluminium is produced was described in *IARC Monograph* Volume 34 (IARC, 1984). The process is briefly summarized here. Since 1886, nearly all aluminium has been produced by electrolysis of alumina dissolved in a molten cryolite (Na_3AlF_6)-based bath (also known as the Hall–Héroult process). Molten aluminium is deposited on the carbon cathode, which also serves as the melt container, and oxygen is simultaneously deposited on and consumes the carbon–carbon anode(s) of the electrolytic cell (Sanders, 2002).

A modern alumina-smelting cell consists of a rectangular steel shell lined with refractory insulation surrounding an inner lining of baked carbon. Electric current enters the cell through the anode (either pre-baked or continuously self-baking Søderberg anode) and leaves through steel (collector) bars connected to the carbon cathode at the bottom. Pre-baked anodes are produced by moulding petroleum coke and coal-tar pitch binder into blocks which are baked at 1000–1200 °C. Søderberg anodes are formed continuously from a paste of petroleum coke and coal-tar pitch. The paste is typically added

Table 1.1 Concentrations of PAHs in the ambient air and in the urine of workers in the aluminium industry[a]

Reference Country	Year of study	Job/task	No. of subjects	No. of samples	No. of smokers	PAH	Air levels (µg/m³)		Urine levels (µmol/mol creatinine)	
							Mean	Range	Mean	Range or SD
Göen *et al.* (1995) Germany	since 1990	Aluminium smelter workers	25	25	NR	1-Hydroxypyrene			[4.2]	[0.05–65]
Schoket *et al.* (1999) Hungary	before 1991	Two aluminium plants	70	NR		1-Hydroxypyrene				
		Plant I	24						4.1	3.6 (SD)
		Plant II	45						22.2	14.2 (SD)
Carstensen *et al.* (1999a), Alexandrie *et al.* (2000) Sweden	1995	Pot-room workers				*Particulate phase*	mg/m³	mg/m³		
			97	97	31%	Total 22	13.2[c]	0.01–270		
			93	93		Benzo[*a*]pyrene	0.97[c]	0.02–23.5		
			94	94		Pyrene	1.11[c]	0.07–34.4		
						Gaseous phase	µg/m³	µg/m³		
			96	96		Total 7	16.3[c]	0.01–132		
			95	95		Pyrene	1.56[c]	0.01–9.5		
						1-Hydroxypyrene				
			94	94		pre-shift			3.4[c]	0.1–26.6
			96	96		post-shift			4.3[c]	0.1–17.7
Friesen *et al.* (2006) Canada	1975–2001	All jobs		CTPV, 2624; B[*a*]P, 1275			CPTV model, 1977–2000	B[*a*]P model, 1977–2000		
		Jobs in pot-room (anode operator/ assistant, controlman, studblast operator, equipment operator, pot operator, foreman)					50–2000	0.2–11		
		Other jobs in pot-rooms					50–700	0.2–11		
		Other jobs, not in pot-rooms					50–150	0.2–0.7		

[a] All studies are for the Søderberg process.

[b] Conversions used: 1-OHP: 1 µmol/mol creatinine = 1.93 µg/g creatinine = 0.013 µmol/l = 2.84 µg/l = 2.84 ng/mL

[c] Median

B[*a*]P, benzo[*a*]pyrene; NR, not reported; SD, standard deviation

to the top of the rectangular steel shell and bakes to form carbon as it passes through the casing, replacing the anode that is being consumed. Molten aluminium is generally removed from the cells daily by siphoning into a crucible (Sanders, 2002).

1.3 Human exposure

Workers in aluminium production are primarily exposed to polycyclic aromatic hydrocarbons (PAHs). Occupational exposures in this industry and the related carbon electrode-manufacturing industry have been monitored most intensively with respect to PAHs. Biomonitoring studies have focused primarily on exposures in the aluminium industry itself (IARC, 1984, 2010; Table 1.1) and in anode-manufacturing for the aluminium industry (IARC, 1984, 2010; Table 1.2). Other potential exposures in these occupational settings include: sulfur dioxide and fluorides; aluminium fluoride; fibrous sodium aluminium tetrafluoride particles; fluorspar; alumina; carbon monoxide; carbon dioxide; various trace metals, such as vanadium, chromium and nickel; asbestos; extreme heat; and high static magnetic fields (Benke *et al.*, 1998; Dufresne *et al.*, 1996).

Exposures to PAHs, sulfur dioxide and fluorides have decreased over time (Benke *et al.*, 1998). At two plants that operated the vertical stud Søderberg pot-rooms in Norway, exposures have decreased fourfold on average between the late 1950s and the late 1980s (Romundstad *et al.*, 1999). The decrease in exposure can be attributed to the implementation of improved control technology, increased use of effective devices for personal protection, and the increasing predominance of pre-bake pot-rooms (Benke *et al.*, 1998), although this may only apply to the anode pre-baking plants. Concentrations of 1-hydroxypyrene in urine of workers in anode-manufacturing for the aluminium industry did not decrease considerably between the mid-1980s and mid-1990s (Table 1.2). In a review of 15 studies, it was concluded that the use of biological monitoring has not led to a reduction in exposure (Hopf *et al.*, 2009). The exposure models by Friesen *et al.* (2006) cover 25 years of extensive monitoring in a Canadian Söderborg smelter, and show a rapid decline in inhalation exposures before the early/mid-1980s, but a considerable levelling off more recently.

Dermal exposure to PAHs and the ensuing uptake through the skin may contribute to the internal exposure of workers to PAHs. Vanrooij *et al.* (1992) showed that dermal exposure does not necessarily correlate with exposure by inhalation of workers in the pot-rooms and the anode pre-bake plants. Levels of benzo[*a*]pyrene on the wrists of workers in the bake-oven area were twice as high as those of workers from the paste plant. The exposure of bake-oven workers to benzo[*a*]pyrene by inhalation, however, appeared to be four times lower than that of workers in the paste plant. Exposure to pyrene by both inhalation and dermal contact was higher in the paste plant. No information was available for temporal trends in dermal exposure in these workplaces.

2. Cancer in Humans

The cancer hazards associated with exposures in aluminium production were evaluated in *IARC Monograph* Volume 92 (IARC, 2010). There was *sufficient evidence* from epidemiological studies of a carcinogenic effect of occupational exposure in aluminium production, based on a relatively large number of studies that showed a consistent excess of cancer of the bladder and a somewhat less consistent excess of lung cancer. The following review is based on studies of aluminium-smelter workers included in *IARC Monograph* Volume 92 (IARC, 2010) and those published later.

Table 1.2 Concentrations of PAHs in the ambient air and in the urine of workers in anode-manufacturing for the aluminium industry

Reference Country Year of study	Job/task	No. of subjects	No. of samples	No. of smokers	PAH	Air levels (µg/m³)		Urinary levels (µmol/mol creatinine)[a]	
						Mean	Range or SD	Mean	Range
Göen *et al.* (1995) Germany	Carbon-electrode production	23	23	NR	1-Hydroxypyrene			[5.8–12.7]	[1.1–65]
Bentsen-Farmen *et al.* (1999) Norway	Electrode paste-plant workers	17	17	NR	Sum of 17 PAHs 1-Hydroxypyrene pre-shift post-shift	38.0	41.6 (SD)	 3.93 10.20	 3.20 (SD) 6.58 (SD)
Friesen *et al.* (2006) Canada 1975–2001						CPTV model, 1977–2000	B[a]P model, 1977–2000		
	carbon plant jobs					50–300	0.2–5		

[a] Conversions used: 1-OHP: 1 µmol/mol creatinine = 1.93 µg/g creatinine = 0.013 µmol/l = 2.84 µg/l = 2.84 ng/mL

B[*a*]P, benzo[*a*]pyrene; CPTV, coal-tar pitch volatiles; SD, standard deviation

2.1 Cancer of the urinary bladder

A large cohort study from Québec, Canada (Gibbs *et al.*, 2007) showed an excess of bladder-cancer mortality with a statistically significant linear trend with cumulative exposure to benzo[*a*]pyrene B[*a*]P (see Table 2.1, available at http://monographs.iarc.fr/ENG/Monographs/vol100F/100F-17-Table2.1.pdf). The excess risk was evident only in workers who had been first employed before 1950, and smaller risks were noted in those first employed later (Gibbs & Sevigny, 2007a, b). An increased risk for bladder cancer and a significant exposure-response trend was found in a cohort study from British Columbia, Canada (Spinelli *et al.*, 2006; Friesen *et al.*, 2007). Both Canadian studies derived smoking-adjusted risk estimates. A significant excess for bladder cancer with a positive exposure-response trend was also found in a study of a Norwegian aluminium smelter (Romundstad *et al.*, 2000). Supporting evidence of a bladder-cancer excess comes from cohort studies from France (Mur *et al.*, 1987; Moulin *et al.*, 2000) and the United States of America (USA) (Rockette & Arena, 1983). A recently reported cohort study from Australia showed no excess of bladder cancer, although the follow-up was relatively short (Friesen *et al.*, 2009; Sim *et al.*, 2009). No bladder-cancer excess was found in a Swedish study (Björ *et al.*, 2008).

2.2 Cancer of the lung

An excess of lung cancer in aluminium-production workers has been reported although the data were less consistent than for bladder cancer. The large Quebec cohort showed a smoking-adjusted excess of lung cancer with an exposure-response trend (Gibbs *et al.*, 2007; Gibbs & Sevigny, 2007b; Armstrong & Gibbs, 2009). An excess of lung cancer, but no clear trend, was noted in the Swedish cohort (Björ *et al.*, 2008). The cohort from British Columbia Canada showed no overall excess of lung cancer, but a trend with increasing cumulative exposure to B[*a*]P (Spinelli *et al.*, 2006; Friesen *et al.*, 2007). The Australian cohort showed no excess but a positive trend with exposure to dust, but not to B[*a*]P (Friesen *et al.*, 2009; Sim *et al.*, 2009). No excess of lung cancer was evident in the studies from France (Mur *et al.*, 1987; Moulin *et al.*, 2000), Norway (Romundstad *et al.*, 2000) or the USA (Rockette & Arena, 1983).

2.3 Synthesis

Overall, the cohort studies strongly support an association between work in aluminium smelters and bladder-cancer risk. Confounding or chance is not likely to explain the findings. There is an increased risk for cancer of the bladder from occupational exposure in aluminium smelters.

An increased risk for lung cancer has been found in several but not all epidemiological studies in the aluminium-production industry. Some studies also show a dose–response trend in terms of B[*a*]P–years. Confounding from smoking or chance is not likely to explain the findings. Based on these observations, there is evidence that risk for cancer of the lung is causally associated with work in aluminium smelters.

The exposure circumstances, especially levels of PAH in aluminium smelters, vary between industrial departments and also depend on the process used. However, data are not sufficient to disentangle the cancer risks associated with these different exposure situations.

3. Cancer in Experimental Animals

Two samples of airborne particulate polynuclear organic matter were collected from two sites in an aluminium-production plant. Each sample was tested by topical application of 50 mg in toluene (1:1) twice weekly to the skin of twenty C3H mice. Samples containing 0.11% and

0.62% B[*a*]P induced 15/18 and 15/17 malignant skin tumours, respectively. The average time of appearance of the first tumours was 24 and 18 weeks, respectively. No tumours were observed in 37 toluene-treated controls (Bingham *et al.*, 1979; IARC, 1984) [Duration of the study and sex of the animals unspecified; the control animals were from a different study of the same laboratory, with the same protocol.]

In addition, several individual polynuclear aromatic compounds for which there is *sufficient evidence* of carcinogenicity in experimental animals have been measured at high levels in air samples taken from certain areas in aluminium-production plants (IARC, 1984, 2010).

4. Other Relevant Data

4.1 Mechanistic evidence relevant to the carcinogenic hazard from occupational exposures during aluminium production

4.1.1 Experimental systems

Air-emission samples from an aluminium-smelting facility were mutagenic in *Salmonella typhimurium* strains TA98 and TA100. All samples were mutagenic in both strains in the presence of an exogenous metabolic activation system and some samples were mutagenic in strain TA98 in the absence of metabolic activation (Alfheim & Wikstrom, 1984). Air-particle samples collected on filters in the anode-paste plant and pot-room in a Søderberg aluminium-production facility were also mutagenic in strains TA100 and TA98, mainly after metabolic activation; some positive results were also obtained in TA98 without S9-mix (Krøkje *et al.*, 1985).

PAHs have been detected and their concentrations measured in the atmosphere of different locations in an aluminium-production plant (IARC, 1984). These PAHs may contribute, in part, to the genotoxic and tumorigenic activities of particulates collected from such plants.

Naphthalene, which is genotoxic and carcinogenic in experimental studies, has also been detected in the indoor atmosphere of an aluminium-production plant (IARC, 2002; Brusick *et al.*, 2008).

4.1.2 Humans

No increase in the frequency of sister chromatid exchange or chromosomal aberrations in peripheral blood lymphocytes was observed in workers in the aluminium industry. No effects on sperm morphology, sperm counts, or double Y-bodies were noted in aluminium-production workers compared with matched controls. There were mixed reports on the mutagenic activity in the urine of workers in the aluminium industry (IARC, 1987).

Human studies on the genotoxic effects of exposures during aluminium production have been reviewed in *IARC Monograph* Volume 92 (IARC, 2010). In several studies, aromatic DNA adducts were analysed in peripheral blood lymphocytes of aluminium-production workers, with mixed results. In 172 Hungarian aluminium-plant workers, higher aromatic DNA-adduct levels were measured compared with those in controls (Schoket *et al.*, 1999). Earlier studies from Hungary had observed aromatic DNA adducts in the lymphocytes of aluminium-plant workers at different locations, at different times of the year, and in different job categories (Schoket *et al.*, 1993a, b, 1995). A significant linear correlation was observed between the total amount of aromatic DNA adducts in lymphocytes and the concentration of 1-hydroxypyrene in urine of Hungarian pot-room workers with the *GSTM1*-null genotype (Schoket *et al.*, 2001). Other populations of aluminium-plant workers have also been studied, with generally positive results with respect to detection of aromatic DNA adducts (Kriek *et al.*, 1993; Ovrebø *et al.*,

1995; van Schooten *et al.*, 1995). Ninety-eight Swedish pot-room workers were examined for the presence of aromatic DNA adducts and gene polymorphisms. No significant differences were observed in the levels of total or individual DNA adducts between pot-room workers and controls (Tuominen *et al.*, 2002). Only one sample from the lymphocytes of 30 aluminium-plant workers was found to contain B[*a*]P-7,8-diol-9,10-oxide-DNA adducts (Vahakangas *et al.*, 1985). In a group of 36 aluminium anode-plant workers, the percentage of subjects with DNA-adduct levels exceeding the 95 percentile control-subject value was small and not significant (Pavanello *et al.*, 1999). Antibodies against B[*a*]P-7,8-diol-9,10-oxide-DNA were detected in the serum of 13.3% of 105 aluminium-plant workers (Galati *et al.*, 2001).

The lymphocytes of 42 Italian aluminium-plant workers were examined for micronucleus formation and DNA-damage induction (single-cell gel electrophoresis assay). While none of the workers showed significant changes in the frequency of micronuclei, significant increases in DNA damage were noted, but only when the lymphocytes were cultured in the presence of cytosine arabinoside, a nucleoside analogue that blocks DNA synthesis (Crebelli *et al.*, 2002).

Ninety-eight Swedish pot-room workers and 55 controls were examined for the presence of polymorphisms in genes encoding biotransformation enzymes, of gene mutations, DNA strand-breaks, and micronuclei in mononuclear blood cells, and of 8-oxodeoxyguanosine in urine. No correlations were found between any of the genotoxicity biomarkers and any of the exposure measures, e.g. length of employment in the pot-room, 1-hydroxypyrene in urine, or PAH-DNA adducts in peripheral lymphocytes, even when different genotypes for biotransformation enzymes were considered (Carstensen *et al.*, 1999b).

4.2 Synthesis

Air-emission samples from aluminium smelters were mutagenic in bacteria. There were mixed reports on the mutagenicity of urine from exposed workers. DNA-adduct studies of blood samples from aluminium-smelter workers also gave mixed results.

Based on both experimental and human studies, there is weak-to-moderate evidence for a genotoxic mechanism underlying the effects of occupational exposures during aluminium production.

5. Evaluation

There is *sufficient evidence* in humans for the carcinogenicity of occupational exposures during aluminium production. Occupational exposures during aluminium production cause cancer of bladder, and of the lung.

There is *sufficient evidence* in experimental animals for the carcinogenicity of airborne particulate polynuclear organic matter from aluminium-production plants.

Air-emission samples from aluminium smelters were mutagenic in bacteria. There were mixed reports on the mutagenicity of urine from exposed workers. DNA-adduct studies of blood samples from aluminium-smelter workers also gave mixed results.

Based on both experimental and human studies, there is weak-to-moderate evidence for a genotoxic mechanism underlying the effects of occupational exposures during aluminium production.

Occupational exposures during aluminium production are *carcinogenic to humans (Group 1)*.

References

Alexandrie A-K, Warholm M, Carstensen U *et al.* (2000). CYP1A1 and GSTM1 polymorphisms affect urinary 1-hydroxypyrene levels after PAH exposure. *Carcinogenesis*, 21: 669–676. doi:10.1093/carcin/21.4.669 PMID:10753202

Alfheim I & Wikstrom L (1984). Air pollution from aluminium smelting plants I. The emission of polycyclic aromatic hydrocarbons and of mutagens from an aluminium smelting plant using the soumlderberg process *Toxicol Environ Chem*, 8: 55–72 doi:10.1080/02772248409357041

Armstrong BG & Gibbs G (2009). Exposure-response relationship between lung cancer and polycyclic aromatic hydrocarbons (PAHs). *Occup Environ Med*, 66: 740–746. doi:10.1136/oem.2008.043711 PMID:19546103

Benke G, Abramson M, Sim M (1998). Exposures in the alumina and primary aluminium industry: an historical review. *Ann Occup Hyg*, 42: 173–189. doi:10.1016/S0003-4878(98)00020-9 PMID:9684558

Bentsen-Farmen RK, Botnen IV, Notø H *et al.* (1999). Detection of polycyclic aromatic hydrocarbon metabolites by high-pressure liquid chromatography after purification on immunoaffinity columns in urine from occupationally exposed workers. *Int Arch Occup Environ Health*, 72: 161–168. doi:10.1007/s004200050355 PMID:10392563

Bingham E, Trosset RP, Warshawsky D (1979). Carcinogenic potential of petroleum hydrocarbons: a critical review of the literature. *J Environ Pathol Toxicol*, 3: 483–563. PMID:397958

Björ O, Damber L, Edström C, Nilsson T (2008). Long-term follow-up study of mortality and the incidence of cancer in a cohort of workers at a primary aluminum smelter in Sweden. *Scand J Work Environ Health*, 34: 463–470. doi:10.5271/sjweh.1293 PMID:19137208

Brusick D, Small MS, Cavalieri EL *et al.* (2008). Possible genotoxic modes of action for naphthalene. *Regul Toxicol Pharmacol*, 51: SupplS43–S50. doi:10.1016/j.yrtph.2007.12.002 PMID:18194829

Carstensen U, Hou SM, Alexandrie AK *et al.* (1999b). Influence of genetic polymorphisms of biotransformation enzymes on gene mutations, strand breaks of deoxyribonucleic acid, and micronuclei in mononuclear blood cells and urinary 8-hydroxydeoxyguanosine in potroom workers exposed to polyaromatic hydrocarbons. *Scand J Work Environ Health*, 25: 351–360. doi:10.5271/sjweh.445 PMID:10505661

Carstensen U, Yang K, Levin J-O *et al.* (1999a). Genotoxic exposures of potroom workers. *Scand J Work Environ Health*, 25: 24–32. doi:10.5271/sjweh.379 PMID:10204667

Crebelli R, Carta P, Andreoli C *et al.* (2002). Biomonitoring of primary aluminium industry workers: detection of micronuclei and repairable DNA lesions by alkaline SCGE. *Mutat Res*, 516: 63–70. PMID:11943612

Dufresne A, Loosereewanich P, Armstrong B *et al.* (1996). Inorganic particles in the lungs of five aluminum smelter workers with pleuro-pulmonary cancer. *Am Ind Hyg Assoc J*, 57: 370–375. doi:10.1080/15428119691014918 PMID:8901239

Friesen MC, Benke G, Del Monaco A *et al.* (2009). Relationship between cardiopulmonary mortality and cancer risk and quantitative exposure to polycyclic aromatic hydrocarbons, fluorides, and dust in two prebake aluminum smelters. *Cancer Causes Control*, 20: 905–916. doi:10.1007/s10552-009-9329-8 PMID:19294522

Friesen MC, Demers PA, Spinelli JJ *et al.* (2007). Comparison of two indices of exposure to polycyclic aromatic hydrocarbons in a retrospective aluminium smelter cohort. *Occup Environ Med*, 64: 273–278. doi:10.1136/oem.2006.028928 PMID:17053015

Friesen MC, Demers PA, Spinelli JJ, Le ND (2006). From expert-based to quantitative retrospective exposure assessment at a Soderberg aluminum smelter. *Ann Occup Hyg*, 50: 359–370. doi:10.1093/annhyg/mel003 PMID:16488921

Galati R, Zijno A, Crebelli R *et al.* (2001). Detection of antibodies to the benzo(a)pyrene diol epoxide-DNA adducts in sera from individuals exposed to low doses of polycyclic aromatic hydrocarbons. *J Exp Clin Cancer Res*, 20: 359–364. PMID:11718215

Gibbs GW, Armstrong B, Sevigny M (2007). Mortality and cancer experience of Quebec aluminum reduction plant workers. Part 2: mortality of three cohorts hired on or before january 1, 1951. *J Occup Environ Med*, 49: 1105–1123. doi:10.1097/JOM.0b013e318157d34a PMID:18000416

Gibbs GW & Sevigny M (2007a). Mortality and cancer experience of Quebec aluminum reduction plant workers, part 4: cancer incidence. *J Occup Environ Med*, 49: 1351–1366. doi:10.1097/JOM.0b013e318156ecbc PMID:18231082

Gibbs GW & Sevigny M (2007b). Mortality and cancer experience of Quebec aluminum reduction plant workers. Part 3: monitoring the mortality of workers first employed after January 1, 1950. *J Occup Environ Med*, 49: 1269–1287. doi:10.1097/JOM.0b013e3181593da8 PMID:17993932

Göen T, Gündel J, Schaller K-H, Angerer J (1995). The elimination of 1-hydroxypyrene in the urine of the general population and workers with different occupational exposures to PAH. *Sci Total Environ*, 163: 195–201. doi:10.1016/0048-9697(95)04484-I PMID:7716499

Hopf NB, Carreon T, Talaska G (2009). Biological markers of carcinogenic exposure in the aluminum smelter industry–a systematic review. *J Occup Environ Hyg*, 6: 562–581. doi:10.1080/15459620903094810 PMID:19629825

IARC (1987). Overall evaluations of carcinogenicity: an updating of IARC Monographs volumes 1 to 42. *IARC Monogr Eval Carcinog Risks Hum Suppl*, 7: 1–440. PMID:3482203

IARC (1984). Polynuclear aromatic compounds, Part 3, industrial exposures in aluminium production, coal gasification, coke production, and iron and steel founding. *IARC Monogr Eval Carcinog Risk Chem Hum*, 34: 1–219.

IARC (2002). Some traditional herbal medicines, some mycotoxins, naphthalene and styrene. *IARC Monogr Eval Carcinog Risks Hum*, 82: 1–556. PMID:12687954

IARC (2010). Some non-heterocyclic polycyclic aromatic hydrocarbons and some related exposures. *IARC Monogr Eval Carcinog Risks Hum*, 92: 1–853. PMID:21141735 PMID:18756632

Kriek E, Van Schooten FJ, Hillebrand MJ *et al.* (1993). DNA adducts as a measure of lung cancer risk in humans exposed to polycyclic aromatic hydrocarbons. *Environ Health Perspect*, 99: 71–75. doi:10.1289/ehp.939971 PMID:8319662

Krøkje A, Tiltnes A, Mylius E, Gullvåg B (1985). Testing for mutagens in an aluminium plant. The results of Salmonella typhimurium tests on expectorates from exposed workers. *Mutat Res*, 156: 147–152. doi:10.1016/0165-1218(85)90057-6 PMID:3889632

Moulin JJ, Clavel T, Buclez B, Laffitte-Rigaud G (2000). A mortality study among workers in a French aluminium reduction plant. *Int Arch Occup Environ Health*, 73: 323–330. doi:10.1007/s004200000124 PMID:10963416

Mur JM, Moulin JJ, Meyer-Bisch C *et al.* (1987). Mortality of aluminium reduction plant workers in France. *Int J Epidemiol*, 16: 257–264. doi:10.1093/ije/16.2.257 PMID:3610453

Ovrebø S, Haugen A, Hemminki K *et al.* (1995). Studies of biomarkers in aluminum workers occupationally exposed to polycyclic aromatic hydrocarbons. *Cancer Detect Prev*, 19: 258–267. PMID:7750114

Pavanello S, Favretto D, Brugnone F *et al.* (1999). HPLC/fluorescence determination of anti-BPDE-DNA adducts in mononuclear white blood cells from PAH-exposed humans. *Carcinogenesis*, 20: 431–435. doi:10.1093/carcin/20.3.431 PMID:10190558

Rockette HE & Arena VC (1983). Mortality studies of aluminum reduction plant workers: potroom and carbon department. *J Occup Med*, 25: 549–557. PMID:6886861

Romundstad P, Andersen A, Haldorsen T (2000). Cancer incidence among workers in six Norwegian aluminum plants. *Scand J Work Environ Health*, 26: 461–469. doi:10.5271/sjweh.569 PMID:11201392

Romundstad P, Haldorsen T, Rønneberg A (1999). Exposure to PAH and fluoride in aluminum reduction plants in Norway: historical estimation of exposure using process parameters and industrial hygiene measurements. *Am J Ind Med*, 35: 164–174. doi:10.1002/(SICI)1097-0274(199902)35:2<164::AID-AJIM8>3.0.CO;2-W PMID:9894540

Sanders RE Jr (2002). *Aluminum and aluminum alloys*. In: *Kirk-Othmer Encyclopedia of Chemical Technology*, 5th ed. New York: John Wiley & Sons [online edition]

Schoket B, Doty WA, Vincze I *et al.* (1993a). Increased sensitivity for determination of polycyclic aromatic hydrocarbon-DNA adducts in human DNA samples by dissociation-enhanced lanthanide fluoroimmunoassay (DELFIA). *Cancer Epidemiol Biomarkers Prev*, 2: 349–353. PMID:8348058

Schoket B, Papp G, Lévay K *et al.* (2001). Impact of metabolic genotypes on levels of biomarkers of genotoxic exposure. *Mutat Res*, 482: 57–69. doi:10.1016/S0027-5107(01)00210-X PMID:11535249

Schoket B, Phillips DH, Poirier MC, Vincze I (1993b). DNA adducts in peripheral blood lymphocytes from aluminum production plant workers determined by 32P-postlabeling and enzyme-linked immunosorbent assay. *Environ Health Perspect*, 99: 307–309. doi:10.2307/3431507 PMID:8319650

Schoket B, Poirier MC, Mayer G *et al.* (1999). Biomonitoring of human genotoxicity induced by complex occupational exposures. *Mutat Res*, 445: 193–203. PMID:10575430

Schoket B, Poirier MC, Vincze I (1995). Biomonitoring of genotoxic exposure in aluminium plant workers by determination of DNA adducts in human peripheral blood lymphocytes. *Sci Total Environ*, 163: 153–163. doi:10.1016/0048-9697(95)04492-J PMID:7716493

Sim MR, Del Monaco A, Hoving JL *et al.* (2009). Mortality and cancer incidence in workers in two Australian prebake aluminium smelters. *Occup Environ Med*, 66: 464–470. doi:10.1136/oem.2008.040964 PMID:19218259

Spinelli JJ, Demers PA, Le ND *et al.* (2006). Cancer risk in aluminum reduction plant workers (Canada). *Cancer Causes Control*, 17: 939–948. doi:10.1007/s10552-006-0031-9 PMID:16841261

Tuominen R, Baranczewski P, Warholm M *et al.* (2002). Susceptibility factors and DNA adducts in peripheral blood mononuclear cells of aluminium smelter workers exposed to polycyclic aromatic hydrocarbons. *Arch Toxicol*, 76: 178–186. doi:10.1007/s00204-002-0331-0 PMID:11967624

Vahakangas K, Haugen A, Harris CC (1985). An applied synchronous fluorescence spectrophotometric assay to study benzo[a]pyrene-diolepoxide-DNA adducts. *Carcinogenesis*, 6: 1109–1115. doi:10.1093/carcin/6.8.1109 PMID:3926334

van Schooten FJ, Jongeneelen FJ, Hillebrand MJX *et al.* (1995). Polycyclic aromatic hydrocarbon-DNA adducts in white blood cell DNA and 1-hydroxypyrene in the urine from aluminum workers: relation with job category and synergistic effect of smoking. *Cancer Epidemiol Biomarkers Prev*, 4: 69–77. PMID:7894326

Vanrooij JGM, Bodelier-Bade MM, De Looff AJA *et al.* (1992). Dermal exposure to polycyclic aromatic hydrocarbons among primary aluminium workers. *Med Lav*, 83: 519–529. PMID:1297067