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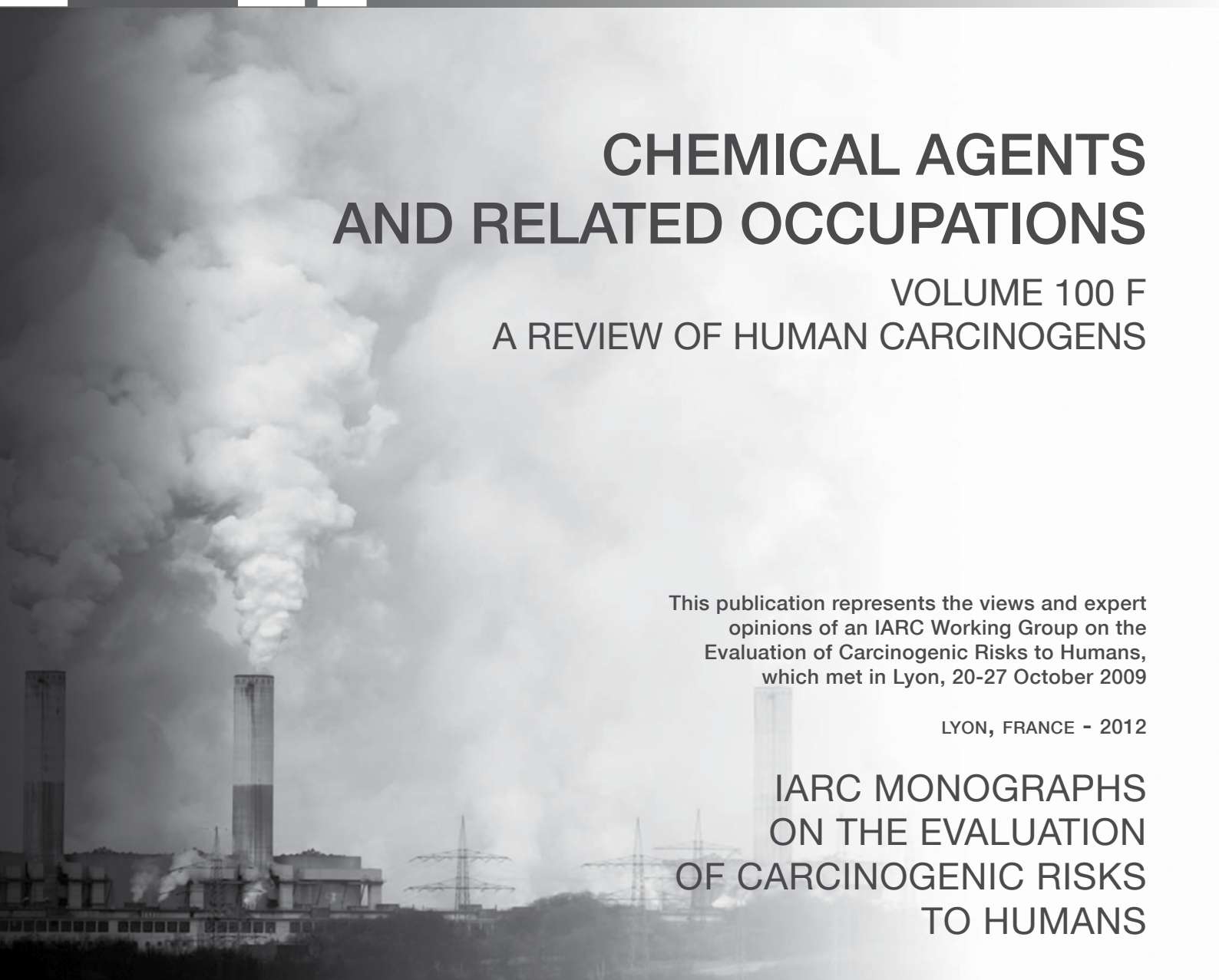

# CHEMICAL AGENTS AND RELATED OCCUPATIONS

## VOLUME 100 F
## A REVIEW OF HUMAN CARCINOGENS

This publication represents the views and expert opinions of an IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, which met in Lyon, 20-27 October 2009

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IARC MONOGRAPHS ON THE EVALUATION OF CARCINOGENIC RISKS TO HUMANS

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# COAL GASIFICATION

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

## 1. Exposure Data

During coal gasification, coal is reacted with oxygen, steam and carbon dioxide to form a gas containing hydrogen and carbon monoxide. During this process, which is essentially incomplete combustion, the heat evolved is consumed and the sulfur and nitrogen in the coal are converted to hydrogen sulfide (rather than sulfur dioxide) and ammonia (rather than nitrogen oxides), respectively. These reduced forms of sulfur and nitrogen are easily isolated, captured and used, making gasification a clean-coal technology with a better environmental performance than coal combustion (Shadle *et al.*, 2002).

Depending on the type of gasifier (e.g. air-blown, enriched oxygen-blown) and the operating conditions, gasification can be used to produce a fuel gas that is suitable for several applications (e.g. low heating-value fuel gas for use as industrial fuel and for power production; medium heating-value fuel gas for use as a synthesis gas in the production of chemicals such as ammonia and methanol, and for transportation fuel; or high heating-value gas) (Shadle *et al.*, 2002).

Gasification takes place in fixed-bed, fluidized-bed, moving-bed, and entrained-flow gasifiers. The earliest gasification processes were developed by use of a counter-current, fixed-bed gasifier, in which coal was fed onto the top of the bed and travelled downwards against the flow of gases. Atmospheric fixed-bed gasifiers of various designs are still occasionally found in small-scale industries. On a large scale, several Lurgi fixed-bed pressurized gasification plants are currently operating commercially, e.g. in the Republic of South Africa and in the USA (Shadle *et al.*, 2002; Crelling *et al.*, 2005). Fluidized-bed gasification, invented in 1922 by Winkler at BASF in Germany, has the advantage of a fairly simple reactor design. In this process, the air and steam flow required for gasification is sufficient to fluidize the bed of coal, char and ash. Fluidization occurs when the gas-flow velocity lifts the particles and causes the gas–solid mixture to flow like a fluid (Shadle *et al.*, 2002; Crelling *et al.*, 2005). Entrained-flow gasification takes place in a flame-like reaction zone, usually at a very high temperature, to produce a liquid slag. For economical operations, a high-standard heat-recovery system is mandatory, but the gas product typically has a very low methane content and is free of tars, oils and phenols, which thereby considerably simplifies gas and water treatment. Entrained-flow gasifiers of the Koppers-Totzek design are operated at atmospheric pressure. They are used industrially in many countries to produce hydrogen or

synthesis gas (Shadle *et al.*, 2002; Crelling *et al.*, 2005).

The moving-bed gasifiers produce tars, oils, phenols and heavy hydrocarbons, and the concentrations in the gas product are controlled by quenching and water scrubbing. Fluidized-bed gasifiers produce significantly smaller amounts of these compounds because of higher operating temperatures. Entrained-flow gasifiers that operate at even higher temperatures (in excess of 1650 °C) can achieve carbon conversions of more than 99.5%, while generating essentially no organic compounds heavier than methane (Shadle *et al.*, 2002).

In addition to PAHs, workers in coal gasification may be exposed to many compounds, including asbestos, silica, amines, arsenic, cadmium, lead, nickel, vanadium, hydrocarbons, sulfur dioxide, sulfuric acid and aldehydes (IARC, 1984).

## 2. Cancer in Humans

### 2.1 Cohort studies of coal-gasification workers

Occupational exposure during coal gasification was evaluated in *IARC Monograph* Volume 92 (IARC, 2010). There was *sufficient evidence* in epidemiological studies for the carcinogenicity of occupational exposure during coal gasification. The main body of evidence came from two cohort studies of coal-gasification workers in the United Kingdom (Doll *et al.*, 1972) and Germany (Berger & Manz, 1992), and a case–control study nested within a cohort of French gas- and electricity-production workers (Martin *et al.*, 2000; see Table 2.1, available at http://monographs.iarc.fr/ENG/Monographs/vol100F/100F-10-Table2.1.pdf). In all studies an excess of lung cancer in association with coal gasification was found, which was not likely to be explained by confounding from tobacco smoking. There was evidence supporting a lung-cancer excess in a historical record-linkage study from the United Kingdom (Kennaway & Kennaway, 1947), in two smaller cohorts (Kawai *et al.*, 1967; Hansen *et al.*, 1986), and a large but inadequately reported Chinese study (Wu, 1988).

In addition to lung cancer, the study from the United Kingdom (Doll *et al.*, 1972) showed an excess of bladder cancer, and the German study (Berger & Manz, 1992) showed an excess of cancers of the stomach and colon-rectum.

No epidemiological studies of coal-gasification workers have been published since the previous evaluation (IARC, 2010).

### 2.2 Synthesis

In three large studies, a consistent excess of lung cancer was found in association with occupational exposure during coal gasification. This excess was not likely to be explained by tobacco smoking.

## 3. Cancer in Experimental Animals

Coal-tars from gas works were previously evaluated in *IARC Monograph* Volume 34 (IARC, 1984). As early as 1923 and in subsequent decades, crude coal-tars from gas-works were tested for carcinogenicity by skin application in six studies in mice and two studies in rabbits. These tars induced a high number of skin papillomas and carcinomas in all studies in mice (Deelman, 1923; Kennaway, 1925; Hieger, 1929; Woglom & Herly, 1929; Berenblum & Schoental, 1947; Grigorev, 1960) and in both studies in rabbits (Berenblum & Schoental, 1947; Grigorev, 1960). No new studies have been published since the previous evaluation.

Manufactured gas plant residues (MGP) were previously evaluated in *IARC Monograph*

## Table 3.1 Carcinogenicity studies in mice exposed to manufactured gas plant residues

| Species, strain (sex)<br>Duration<br>Reference | Route<br>Dosing regimen,<br>Animals/group at start | Incidence of tumours | Significance | Comments |
|---|---|---|---|---|
| Mouse, B6C3F$_1$ (M, F)<br>185 d<br>Weyand *et al.* (1994) | Groups of 10 male and 10 female mice were fed a gel diet containing 0 (control) or 0.50% MGP. | Fore-stomach carcinomas (M): 0/10, 1/10<br>Alveolar epithelium hyperplasia (M): 0/10, 1/10 | NS | |
| Mouse, A/J (F)<br>260 d<br>Weyand *et al.* (1995) | Groups of 30 mice were fed a gel diet containing 0 (control), 0.1, or 0.25% MGP. | Lung adenoma: 4/19, 19/27*, 29/29*<br>Lung adenoma multiplicity: 0.59, 1.19**, 12.17** tumours/mouse | *$P < 0.05$<br>**$P < 0.001$ | Authors could not explain the decrease in body weight gain that led to increased mortality in basal gel diet controls. No fore-stomach tumours were observed. |
| Mouse, B6C3F$_1$ (F)<br>104 wk<br>Culp *et al.* (1998) | Groups of 48 mice were fed a diet containing 0 (control), 0.01, 0.03, 0.1, 0.3, 0.6 or 1.0% of CT-1. Additional groups of 48 mice were fed a diet containing 0.03, 0.1 or 0.3% of CT-2. | Hepatocellular adenomas or carcinomas (mainly adenomas)**: 0/47, 4/48, 2/46, 3/48, 14/45*, 1/42, 5/43, 7/47, 4/47, 10/45*<br>Alveolar/bronchiolar adenomas or carcinomas (mainly adenomas)**: 2/47, 3/48, 4/48, 4/48, 27/47*, 25/47*, 21/45*, 4/48, 10/48*, 23/47*<br>Fore-stomach papillomas or carcinomas**: 0/47, 2/47, 6/45, 3/47, 14/46*, 15/45*, 6/41, 3/47, 2/47, 13/44*<br>Fore-stomach carcinomas**: 0/47, 0/47, 0/45, 2/47, 7/46*, 10/45*, 4/41, 0/47, 1/47, 6/44*<br>Small intestine adenocarcinomas***: 0/47, 0/46, 0/45, 0/47, 0/42, 22/36*, 36/41*, 0/47, 0/47, 1/37<br>Haemangiosarcomas**: 1/48, 0/48, 1/48, 1/48, 11/48*, 17/48*, 1/45, 1/48, 4/48, 17/48*<br>Histiocytic sarcomas**: 1/48, 0/48, 0/48, 1/48, 7/48, 5/48, 0/45, 3/48, 2/48, 11/48*<br>Sarcomas**: 1/48, 4/48, 3/48, 2/48, 7/48, 1/48, 2/45, 0/48, 4/48, 5/48 | *$P < 0.05$<br>**$P$–value for dose-related trend significant (0.003-< 0.00001) for CT-1 and CT-2<br>***$P$–value for dose related trend < 0.00001 for CT-1 | CT-1 was a composite from seven MGP waste sites. CT-2 was a composite from two of the seven waste sites plus a third site that had a very high benzo[*a*]pyrene content.<br>Haemangiosarcomas included those of the skin, mesentery, mesenteric lymph nodes, heart, spleen, urinary bladder, liver, uterus, thoracic cavity, ovary and skeletal muscle.<br>Sarcomas included those of the mesentery, fore-stomach, skin and kidney. |

**Table 3.1 (continued)**

| Species, strain (sex) Duration Reference | Route Dosing regimen, Animals/group at start | Incidence of tumours | Significance | Comments |
|---|---|---|---|---|
| Mouse, B6C3F$_1$ (M) 52 wk Rodriguez *et al.* (1997) | Groups of more than 30 mice were administered a single intraperitoneal injection of 1.995, 3.99, 7.98 mg MGP-7 or 7.98 mg MGP-4 in corn oil. A group of approximately 60 mice served as corn-oil controls. | Liver tumours (mainly adenomas): 4/34, 8/32*, 17/29*, 12/28*, 3/63 | *[$P < 0.01$] | MGP-4 from a single MGP site. MGP-7 was a composite of seven MGP sites including site MGP-4. No fore-stomach tumours and few pulmonary adenomas were observed. |

CT-1, coal tar mixture 1; d, day or days; F, female; M, male; MGP, manufactured gas plant residues; NS, not significant; wk, week or weeks

Volume 92 (IARC, 2010). MGP were tested in one feeding study in female B6C3F$_1$ mice, one feeding study in female A/J mice, one feeding study in B6C3F$_1$ mice of both sexes, and in one study in male B6C3F$_1$ mice that received the agent by intraperitoneal injection (Table 3.1). In the first feeding study, an increased incidence of hepatocellular adenomas and carcinomas combined, alveolar/bronchiolar adenomas and carcinomas combined, forestomach papillomas and carcinomas, small intestine adenocarcinomas, as well as haemangiosarcomas, histiocytic sarcomas, and sarcomas were observed in female B6C3F$_1$ mice (Culp *et al.*, 1998). In the second study, female A/J mice developed lung adenomas at an increased incidence and multiplicity (Weyand *et al.*, 1995). The third study, in male and female B6C3F$_1$ mice, did not show an increase in tumour incidence (Weyand *et al.*, 1994). In male mice, intraperitoneal injection of MGP produced a significant increase in liver tumours, mostly adenomas (Rodriguez *et al.*, 1997). No new studies have been published since the previous evaluation.

## 4. Other Relevant Data

### 4.1 Mechanistic evidence relevant to the carcinogenic hazards from occupational exposures during coal gasification

#### *4.1.1 Experimental systems*

As reported in *IARC Monograph* Volume 34 (IARC, 1984), coal-gasification samples from the process stream and waste by-products were found to be mutagenic in various strains of *Salmonella typhimurium* in the presence of an exogenous metabolic activation system. The mutagenicity was found primarily in the fractions containing polycyclic aromatic hydrocarbons and their alkylated derivatives. The basic and neutral fractions of tar condensed from a product-gas stream induced both 6-thioguanine-resistant and 8-azaadenine-resistant mutations in DNA repair-deficient Chinese hamster ovary cells in the presence of exogenous metabolic activation. However, neither the micronucleus frequency nor the number of chromosomal aberrations were significantly increased by this treatment.

Male B6C3F1 mice were fed a diet containing coal tar from a gas plant residue. A complex pattern of aromatic adducts was observed in liver, lung, and fore-stomach DNA of these animals, which increased with dose and duration of treatment. In lung DNA one adduct was tentatively identified as *anti*-benzo[*a*]pyrene-7,8-diol-9,10-oxide-deoxyguanosine. This adduct was also identified in fore-stomach DNA from female B6C3F1 mice fed coal tar-containing diets (Culp & Beland, 1994). The identity of this adduct was confirmed upon analysis of lung DNA of female B6C3F1 mice fed a diet containing coal tar from manufactured gas plant residue. However, based on the levels of this specific adduct it was suggested that benzo[*a*]pyrene (B[*a*]P) contributes only a small fraction to the DNA adducts formed in lung tissue of mice that were given coal tar (Beland *et al.*, 2005). Male B6C3F1 mice were fed diets containing 0.1–1% (w/w) coal tar for 15 days. Adduct formation in the lung, but not in the fore-stomach, was dose-related. The B[*a*]P content in the coal tar could not account by itself for the aromatic DNA-adduct levels measured (Weyand *et al.*, 1991). Strain A/J mice formed aromatic DNA adducts in the lungs after ingestion of coal tar from manufactured gas plant residue via the diet. Three major DNA adducts were identified as being derived from benzo[*b*]fluoranthene, benzo[*a*]pyrene, and benzo[*c*]fluorene (Koganti *et al.*, 2000; Koganti *et al.*, 2001). In another study, female ICR mice received topical application of manufactured gas plant residue. In the complex pattern of lung DNA adducts, one was identified as being derived from 7H-benzo[*c*]fluorene.

However, detailed quantitative results after chromatographic separation of the residue into seven fractions suggested that components other than 7H-benzo[*c*]fluorene played an important role in adduct formation in lung DNA (Cizmas *et al.*, 2004). A retrospective comparison of tumour induction and DNA-adduct formation by B[*a*]P and coal tars in several experimental protocols indicated that tumour outcomes were not predicted by the formation of total DNA adducts or by the DNA adducts formed by B[*a*]P. These data suggest that B[*a*]P content by itself is not predictive of tumour outcome (Goldstein *et al.*, 1998).

In *IARC Monograph* Volumes 32 and 92 (IARC, 1983, 2010), benzo[*b*]fluoranthene was evaluated and found to be both genotoxic and carcinogenic in experimental studies. 7H-benzo[*c*]fluorene was carcinogenic to mice (IARC, 2010), but gave inconclusive results as a bacterial mutagen in *Salmonella typhimurium* strains TA98 and TA100 in the presence of an Aroclor-1254-induced rat-liver S9 (IARC, 1983). While a 7H-benzo[*c*]fluorene-DNA adduct was observed in mice that received topical applications of manufactured gas plant residue (Cizmas *et al.*, 2004), the structure of this adduct is unknown, although a diol epoxide structure has been proposed (Wang *et al.*, 2002).

Polycyclic aromatic hydrocarbons in the ambient air in gas works have been analysed (IARC, 1984) and several of these have been shown to be mutagenic (i.e. benz[*a*]anthracene, benzo[*a*]pyrene, benzo[*ghi*]perylene) and carcinogenic (i.e. benz[*a*]anthracene, benzo[*a*]pyrene) in experimental studies (IARC, 1983, 2010; Platt & Grupe, 2005; Platt *et al.*, 2008a, b). These polycyclic aromatic hydrocarbons may contribute to the genotoxic and tumorigenic activities of tars from coal gasification.

Naphthalene has been reported to be a constituent of tar from coal gasification (IARC, 1984). Naphthalene is genotoxic and induces tumours in experimental animals (IARC, 1982; Brusick *et al.*, 2008).

### *4.1.2 Humans*

There are no studies that describe specific effects in workers exposed to emissions associated with coal gasification.

## 4.2 Synthesis

There is strong evidence from experimental studies for a genotoxic mode of action for coal-gasification samples. Although there are no human studies, it is highly likely that genotoxicity is the mechanism relevant to the carcinogenic hazards from exposures to emissions of coal gasification.

# 5. Evaluation

There is *sufficient evidence* in humans for the carcinogenicity of coal gasification. Coal gasification causes cancer of the lung.

There is *sufficient evidence* in experimental animals for the carcinogenicity of coal-tars from gas-works and manufactured gas plant residues.

There is strong evidence for a genotoxic mechanism for coal gasification samples based on experimental studies. Although there are no human studies, it is highly likely that genotoxicity is the mechanism for the carcinogenic effects of coal-gasification emissions, predominantly due to the presence of mutagenic PAHs.

Coal gasification is *carcinogenic to humans (Group 1).*

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