



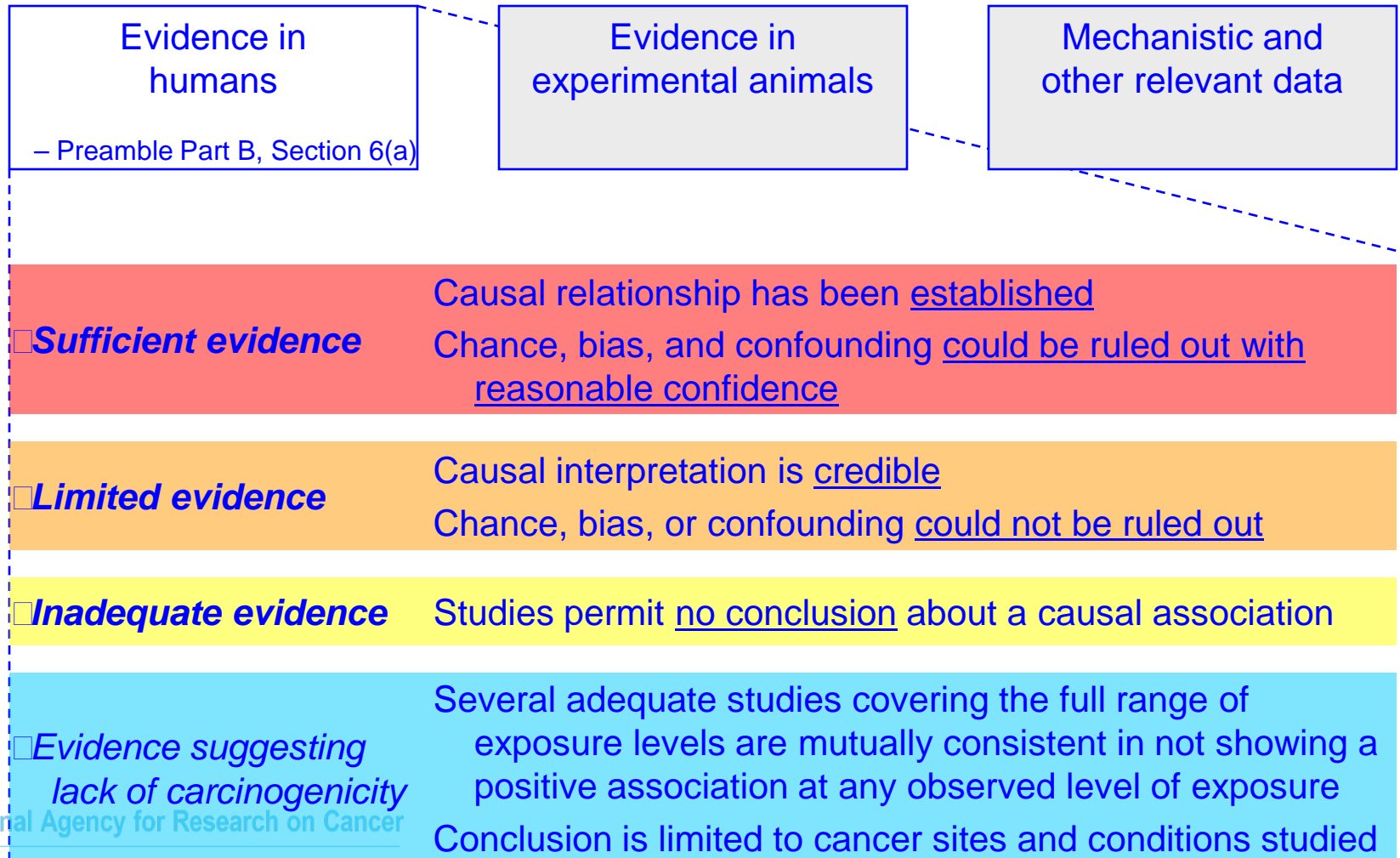
# Non-ionizing radiation, Part II, Radiofrequency Electromagnetic Fields *IARC Monographs, Vol 102*

International Agency for Research on Cancer  
Lyon, France

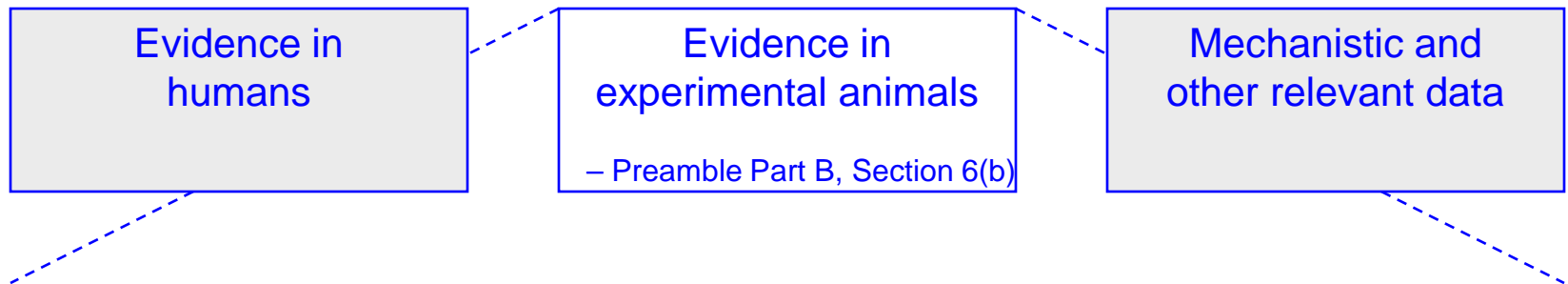
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# Evaluating human data



# Evaluating experimental animal data



**Sufficient evidence** Causal relationship has been established through either:  
- Multiple positive results (2 species, studies, sexes of GLP)  
- Single unusual result (incidence, site/type, age, multi-site)

**Limited evidence** Data suggest a carcinogenic effect but: (e.g.) single study, benign tumours only, promoting activity only

**Inadequate evidence** Studies permit no conclusion about a carcinogenic effect

**Evidence suggesting lack of carcinogenicity** Adequate studies in at least two species show that the agent is not carcinogenic  
Conclusion is limited to the species, tumour sites, age at exposure, and conditions and levels of exposure studied

# Overall evaluation

		EVIDENCE IN EXPERIMENTAL ANIMALS			
		<i>Sufficient</i>	<i>Limited</i>	<i>Inadequate</i>	<i>ESLC</i>
EVIDENCE IN HUMANS	<i>Sufficient</i>	Group 1			
	<i>Limited</i>	↑ 1 <u>strong evidence in exposed humans</u> Group 2A	↑ 2A belongs to a mechanistic class where other members are classified in Groups 1 or 2A Group 2B (exceptionally, Group 2A)		
	<i>Inadequate</i>	↑ 1 <u>strong evidence in exposed humans</u> ↑ 2A <u>strong evidence ... mechanism also operates in humans</u> Group 2B ↓ 3 <u>strong evidence ... mechanism does not operate in humans</u>	↑ 2A belongs to a mechanistic class ↑ 2B with <u>supporting evidence from mechanistic and other relevant data</u> Group 3	↑ 2A belongs to a mechanistic class ↑ 2B with <u>strong evidence from mechanistic and other relevant data</u> Group 3	Group 3 ↓ 4 <u>consistently and strongly supported by a broad range of mechanistic and other relevant data</u>
	<i>ESLC</i>	Group 3			Group 4

# Radiofrequency Electromagnetic Fields Exposure

Human exposure to RF-EMF can occur from

## Environmental sources

- broadcast antennas, base stations, medical devices

## Occupational sources

- high-frequency dielectric and induction heaters, radars

## Personal devices

- cordless telephones, mobile telephones, Bluetooth

The general population receives the **highest exposure** to RF-EMF from **sources in close vicinity to the body**

# Radiofrequency Electromagnetic Fields Exposure, contd

Holding a **mobile phone** to the ear can result in high specific absorption rate (SAR) values in the brain, depending on the positioning of the phone and its antenna and the **quality of the link with the base-station**.

For **children**, the average deposition of RF energy from a mobile phone is about **two-fold higher** in the brain and up to 10-fold higher in the bone marrow of the skull.

The use of **hands-free kits lowers exposure to the brain to <10%** of the value resulting from use at the ear, but it may increase exposure in other parts of the body.

# Radiofrequency Electromagnetic Fields

## Epidemiological data

Occupational exposure to RF-EMF involves

- military and security personnel using walkie-talkies
- radar operators and maintenance personnel
- radio/TV antenna maintenance and repair workers
- workers in dielectric welding, and in sealing of plastics
- physiotherapists applying diathermy treatments

Only very few studies made an attempt to verify or measure exposure to RF-EMF, and in many studies there may have been also exposure to ELF-EMF

# Radiofrequency Electromagnetic Fields

## Epidemiological data, contd

Occupational exposure to RF-EMF: some positive signals

<u>Brain cancer</u>	<u>cases/controls</u>	<u>relative risk (95%CI)</u>
Thomas <i>et al.</i> 1987	435/386	1.7 (1.1-2.7)

A death-certificate-based case-control study, with job title as proxy for exposure to RF-EMF. The excess risk attenuated when those exposed to soldering fumes or lead were excluded, with OR, 1.4 (0.7-3.1).

Grayson <i>et al.</i> 1996	230/920	1.39 (1.01-1.90)
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A large case-control study among US Airforce personnel exposed to equipment producing RF-EMF. Exposure assessment relied on job title and time of deployment, cancer cases were taken from hospital discharge records, but were not confirmed.

# Radiofrequency Electromagnetic Fields

## Epidemiological data, contd

### Environmental exposure to RF-EMF

Ecological and case-control studies have been carried out to investigate potential associations of **brain cancer** with RF emissions from transmission antennae.

These studies are generally limited by reliance on measures of geographic proximity to the antennae as an exposure surrogate. **Substantial exposure misclassification** is unavoidable.

For the same reason, no conclusions can be drawn from the limited data that were available on risk for **leukaemia**, **lymphoma**, or several other cancers.

# Radiofrequency Electromagnetic Fields

## Epidemiological data, contd

Three types of study addressed the question of increased cancer risk and **mobile phone use**

- **Ecological studies** on time trends of disease rates

These analyses covered the period of the late 1990s and early 2000s, i.e. before mobile phone use became widespread

- **Cohort study**

A total of 257 cases of glioma were found in 420,095 subscribers to two Danish telephone companies, with 253.9 expected. Subscription was taken as a surrogate for phone use.

- **Case-control studies**

So far, these studies provide the most informative results

# Radiofrequency Electromagnetic Fields

## Epidemiological data, contd

### Case-control studies on mobile phone use

The **INTERPHONE** study, a multicentre case-control study, is the largest investigation so far of mobile-phone use and brain tumours, including glioma, acoustic neuroma, and meningioma.

The pooled analysis included 2708 **glioma cases** and 2972 controls (participation rates 64% and 53%, resp). Ever/never use of a mobile phone yielded an OR of 0.81 (0.70-0.94). ORs were below or close to unity for all deciles of exposure except the highest decile (**>1640 hours of cumulative call time**) with an **OR of 1.40 (1.03-1.89)**.

# Radiofrequency Electromagnetic Fields

## Epidemiological data, contd

### Case-control studies on mobile phone use (contd)

In a recent study (Cardis, *in press*, *OEM*), estimates of RF energy deposition at the centre of the brain tumours were used as a measure of RF dose. An increased risk for glioma was seen in the highest quintile, and an increasing trend with increasing RF dose for exposures >7 years in the past.

<u>TCSE (J/kg)</u>	<u>OR (95% CI)</u>	
<76.7	1.11 (0.61-2.02)	
76.7-	1.53 (0.85-2.78)	
284.1-	1.50 (0.81-2.78)	
978.9-	1.69 (0.91-3.13)	
3123.9+	1.91 (1.05-3.47)	( $p_{\text{trend}} = 0.01$ )

# Radiofrequency Electromagnetic Fields

## Epidemiological data, contd

A pooled analysis from Sweden included 1148 glioma cases (ascertained 1997–2003) and 2438 controls, obtained through cancer and population registries, respectively.

Questionnaires and telephone interviews were used to obtain information on the exposures and covariates of interest, including use of mobile and cordless phones (response rates 85% and 84%, respectively).

Participants who had used a mobile phone for more than 1 year had an OR for glioma of 1.3 (95% CI 1.1-1.6), which increased with longer time since first use and with total call time, reaching 3.2 (2.0–5.1) for > 2000 hours of use (Hardell et al, 2011).

# Radiofrequency Electromagnetic Fields

## Epidemiological data, contd

Although both the INTERPHONE study and the Swedish pooled analysis are susceptible to bias, the Working Group concluded that the findings could not be dismissed as reflecting bias alone, and that a causal interpretation is possible.

A similar conclusion was drawn from these two studies for **acoustic neuroma**, although the case numbers were substantially smaller than for glioma.

Additionally, a study from Japan found evidence of an increased risk for **acoustic neuroma** associated with ipsilateral mobile phone use.

# Radiofrequency Electromagnetic Fields

## Epidemiological data, contd

For **meningioma**, parotid-gland tumours, leukaemia, lymphoma, and other tumour types, the Working Group found the available evidence insufficient to reach a conclusion on the potential association with mobile phone use.

The Working Group concluded that there is *limited evidence* in humans for the carcinogenicity of RF-EMF, based on positive associations between **glioma** and **acoustic neuroma** and exposure to RF-EMF from wireless phones.

Note: a few members of the Working Group considered the current evidence in humans *inadequate*.

# Radiofrequency Electromagnetic Fields

## Cancer in experimental animals

The Working Group reviewed **more than 40 studies** that assessed the carcinogenicity of RF-EMF in rodents. Exposures included 2450-MHz RF-EMF and various RF-EMF types that simulated emissions from mobile phones.

**None of the seven chronic bioassays** showed an increased incidence of any tumour type in animals exposed to RF-EMF for 2 years. An increased total number of malignant tumours was found in one of these chronic bioassays.

**Increased cancer incidences** were noted

- in two of 12 studies with tumour-prone animals
- in one of 18 studies with initiation-promotion protocols
- in four of six co-carcinogenesis studies after exposure to RF-EMF in combination with a known carcinogen.

The Working Group concluded that there is **limited evidence in experimental animals** for the carcinogenicity of RF-EMF.

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# Radiofrequency Electromagnetic Fields

## Mechanistic and other relevant data

The Working Group reviewed many studies with endpoints relevant to **mechanisms of carcinogenesis**, including

- Genotoxicity
- Effects on immune function
- Gene and protein expression
- Cell signalling
- Oxidative stress
- Apoptosis
- Effects on the blood-brain barrier
- Other effects in the brain

There was evidence of an effect of RF-EMF on some of these endpoints, but the results provided only **weak mechanistic evidence relevant to RF-EMF-induced cancer in humans**.

# Radiofrequency Electromagnetic Fields

## Overall evaluation

# THE LANCET Oncology

News

## Carcinogenicity of radiofrequency electromagnetic fields



In May, 2011, 30 scientists from 14 countries met at the International Agency for Research on Cancer (IARC) in Lyon, France, to assess the carcinogenicity of radiofrequency electromagnetic fields (RF-EMF). These assessments will be published as Volume 102 of the IARC Monographs.<sup>1</sup>

induced electric and magnetic fields and associated currents inside tissues. The most important factors that determine the induced fields are the distance of the source from the body and the output power level. Additionally, the efficiency of coupling and resulting field distribution inside

regarding associations between use of wireless phones and glioma.

The cohort study<sup>4</sup> included 257 cases of glioma among 420095 subscribers to two Danish mobile phone companies between 1982 and 1995. Glioma incidence was near the national average for the subscribers. In this study,



The IARC Working Group concluded that there is

- **limited evidence in humans** for the carcinogenicity of RF-EMF, based on positive associations between glioma and acoustic neuroma and exposure to RF-EMF from wireless phones.
- **limited evidence** in experimental animals for the carcinogenicity of RF-EMF.
- **weak mechanistic evidence** relevant to RF-EMF-induced cancer in humans.

Overall, RF-EMF were classified as “**possibly carcinogenic to humans**” (Group 2B).

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# Carcinogenicity of chemicals in industrial & consumer products, food contaminants & flavourings, & water chlorination byproducts , Vol 101, Oct 2011

Most assessments relied mainly on **carcinogenicity bioassays**. The **relevance to humans** of the tumours reported in these studies was discussed with regard to mechanisms of carcinogenesis, such as peroxisome proliferation and PPARalpha activation, alpha2u-globulin nephropathy, and metabolism via CYP2F enzymes.

## **2-nitrotoluene**

- **Occupational exposure** to 2-nitrotoluene occurs during production of dyes, rubber chemicals, agricultural chemicals, and explosives.
- it caused an **unusually high incidence of tumours in rats**, including fibrosarcomas of the skin, malignant mesotheliomas, mammary gland fibroadenomas (also in male rats), and cholangiocarcinomas. Even **short exposures of 13 or 26 weeks** caused cancer in rats. In mice, unusually high incidences of carcinomas of the caecum and haemangiosarcomas are noted.
- In view of **strong mechanistic considerations**, and extraordinarily **early onset and high tumour incidences** reported, 2-nitrotoluene was classified in **Group 2A**, “probably carcinogenic to humans”.

# Carcinogenicity of chemicals in industrial & consumer products, food contaminants & flavourings, & water chlorination byproducts , Vol 101, Oct 2011, DEHP

DEHP is widely used as a **plasticiser**. The general population is exposed to DEHP through leaching from plastic medical devices, such as blood bags and medical tubing, and as a contaminant of food packaged in DEHP-containing materials.

- DEHP was **tested for carcinogenicity** by oral exposure in mice and rats; hepatocellular adenomas and carcinomas were increased in both species. Additional studies found an increased incidence of pancreatic acinar-cell adenomas in male rats, and increased incidence of Leydig-cell tumours in rats.
- Data from **new mechanistic studies suggest that many molecular signals and pathways in several cell types** in the liver, rather than a single molecular event, contribute to cancer development in rodents.
- The WG concluded that the human relevance of the molecular events leading to DEHP induced cancer in several target tissues (eg, liver and testis) in rats or mice could not be ruled out, resulting in the **evaluation of DEHP in Group-2B**.

# Occupational exposures to bitumens and their emissions, Vol 103, Oct 2011

**Bitumens** are produced by distillation of crude oil during petroleum refining, and also occur naturally. Bitumens can be divided into broad classes according to their physical properties and specifications required for the different uses. The major use of bitumens is in **asphalt for road paving**; other uses include **roofing, waterproofing**, and sealing and painting.

- Occupational exposures to oxidized bitumens and their emissions during roofing are '**probably carcinogenic to humans**' (Group 2A);
- Occupational exposures to hard bitumens and their emissions during mastic asphalt work are '**possibly carcinogenic to humans**' (Group 2B)
- Occupational exposures to straight-run bitumens and their emissions during road paving are '**possibly carcinogenic to humans**' (Group 2B).

# Forthcoming IARC Monographs

- *Volume 104*: Polyomaviruses (SV40, BK, JC, and Merkel cell viruses) and malaria: 7-14 Feb 2012
- *Volume 105*: Diesel and gasoline engine exhausts and some nitroarenes: 5-12 June 2012

# Volume 100<sup>+</sup>, April & Nov 2012

- *Tumour (Site) Concordance between Humans and Animals*
  - Increase understanding of the correspondence across species
  - Identify human cancer sites without good animal models
- *Mechanisms Involved in Human Carcinogenesis*
  - Organized by mechanism to facilitate joint consideration of agents that act through similar mechanisms
  - Identify biomarkers that could be influential in future studies
  - Identify susceptible populations and developmental stages
  - Promote research that will lead to more confident evaluations



**Thank you!**

International Agency for Research on Cancer



# Radiofrequency Electromagnetic Fields

## (Epidemiological data, contd)

### Occupational exposure to RF-EMF: some positive signals

#### Leukaemia/lymphoma cohort relative risk (95%CI)

Lagorio *et al* 1997 682 5.0 (1.3-27.9)

A mortality study among workers in a plastic-ware industry, with exposure to RF-EMF (during sealing), and to vinyl chloride monomer. The study is small, possible confounding is not addressed.

Degrave *et al* 2009 2932 7.2 (1.1-48.9)

Cause-specific mortality study among Belgian soldiers in batallions equipped with radar. Follow-up problematic; co-exposure to ionizing radiation suggested

#### Testicular cancer cases/controls relative risk (95%CI)

Hayes *et al.* 1990 271/259 3.1 (1.4-6.9)

Hospital-based case-control study. Controls had cancer, but not in the genital tract. Exposure classification was based on self-reporting, probably with substantial misclassification.

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# Radiofrequency Electromagnetic Fields (Epidemiological data, contd)

## Case-control studies on mobile phone use

Muscat *et al* 2000, Inskip *et al* 2001, Auvinen *et al* 2002

Early studies in the period of increasing use, with exposure assessment by self-reported history or by subscription records, and imprecise effect estimates.

	<u>Phone type</u>	<u>Odds ratio (95%CI)</u>
Glioma (n=398)	all phones	1.5 (1.0-2.4)
	digital	1.0 (0.5-2.0)
	analog	2.1 (1.3-3.4)

from: Auvinen *et al*, 2002

# Radiofrequency Electromagnetic Fields (Overall evaluation)

## Cancer in Humans

There is *limited evidence* in humans for the carcinogenicity of RF-EMF, based on positive associations between glioma and acoustic neuroma and exposure to RF-EMF from wireless phones.

## Cancer in Experimental Animals

There is *limited evidence* in experimental animals for the carcinogenicity of RF-EMF.

## Overall Evaluation

Radiofrequency electromagnetic fields are *possibly carcinogenic to humans (Group 2B)*.

# The *IARC Monographs*

## Acknowledgements

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- U.S. National Cancer Institute (since 1982)
- European Commission, DG for Employment, Social Affairs and Equal Opportunities (since 1986)
- U.S. National Institute of Environmental Health Sciences (since 1992)
- U.S. Environmental Protection Agency (since 2001)

# Occupational exposures to bitumens and their emissions, Vol 103, Oct 2011

Occupational exposures to oxidized bitumens and their emissions during roofing

The body of available data from cancer studies in humans points to an association between exposures to oxidized bitumens during roofing and lung cancer. In support of these findings, extracts and fume condensates of oxidized bitumens, which are used primarily in roofing applications, showed *sufficient evidence* of carcinogenicity in 2-year bioassays.

Overall, the Working Group evaluated occupational exposures to oxidized bitumens and their emissions during roofing as “probably carcinogenic to humans” Group 2A

# Occupational exposures to bitumens and their emissions, Vol 103, Oct 2011

Occupational exposures to **hard bitumens and their emissions during mastic asphalt work**

Based on **two positive studies among mastic asphalt workers**, the Working Group concluded that there was ***limited evidence in humans*** for the carcinogenicity of occupational exposures during mastic asphalt work. This type of bitumens has not been tested in experimental animals.

In consequence, occupational exposures to **hard bitumens and their emissions during mastic asphalt work** were classified as **“possibly carcinogenic to humans” (Group 2B)**.

# Occupational exposures to bitumens and their emissions, Vol 103, Oct 2011

Occupational exposures to straight-run bitumens and their emissions during road paving

There was *inadequate evidence in humans* for the carcinogenicity of occupational exposures during road paving with straight-run bitumens.

There was *inadequate evidence in experimental animals* for the carcinogenicity of extracts and of fume condensates of this type of bitumens.

Studies of workers exposed to bitumen emissions during paving with straight-run bitumens showed *mutagenic and genotoxic/cytogenetic effects in these workers*. Similar effects were observed in experimental systems under controlled conditions. This *strong mechanistic evidence* led to the classification of occupational exposures to straight-run bitumens and their emissions during road paving as “possibly carcinogenic to humans” (Group 2B).