IARC Monographs, Vol 98, 2007
Occupational Exposure as a Firefighter

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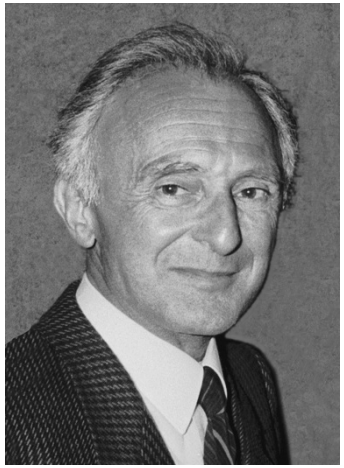
International Agency for Research on Cancer
Lyon, France

DGUV, St. Augustin, 3 November 2015

“The encyclopaedia of carcinogens”

The *IARC Monographs* evaluate

- Chemicals
- Complex mixtures
- Occupational exposures
- Physical and biological agents
- Lifestyle factors



Lorenzo Tomatis
1929-2007

More than 950 agents have been evaluated

- 118 are *carcinogenic to humans* (Group 1)
- 75 are *probably carcinogenic to humans* (Group 2A)
- 288 are *possibly carcinogenic to humans* (Group 2B)

National and international health agencies use the *Monographs*

- As a source of scientific information on known or suspected carcinogens
- As scientific support for their actions to prevent exposure to known or suspected carcinogens

Since 1971 over 1000 scientists from over 50 countries have contributed their expertise to the IARC Monographs

WHO Declaration of Interests

To ensure public confidence that interested parties do not have links to the WG, IARC strives to identify and avoid real or apparent conflicts of interests

- Before official invitation WG have to declare employment, research, and financial interests
- At the opening of the meeting they are asked to update their Declaration

Pertinent interests are disclosed

- To meeting participants
- To the public ((http://monographs.iarc.fr/)
- In the published volume of *Monographs*

They are asked also to complete the conflict-of-interest form required by *The Lancet Oncology*

- IARC sends *TLO*'s form — not WHO's form — to *TLO;*
- *TLO* summarizes this information alongside IARC's summary

Evaluating human data (Subgroup 2)

Cancer in humans — Preamble Part B, Section 6(a)	Cancer in experimental animals	Mechanistic and other relevant data

Sufficient evidence	Causal relationship has been established Chance, bias, and confounding could be ruled out with reasonable confidence
Limited evidence	Causal interpretation is credible Chance, bias, or confounding could not be ruled out
Inadequate evidence	Studies permit no conclusion about a causal association
Evidence suggesting lack of carcinogenicity	Several adequate studies covering the full range of exposure levels are mutually consistent in not showing a positive association at any observed level of exposure Conclusion is limited to cancer sites and conditions studied

Evaluating experimental animal data (Subgroup 3)

Cancer in humans	Cancer in experimental animals — Preamble Part B, Section 6(b)	Mechanistic and other relevant 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

Evaluating mechanistic and other data (Subgroup 4)

Cancer in humans	Cancer in experimental animals	Mechanistic and other relevant data — Preamble Part B, Section 6(c)

- Are the mechanistic data “weak,” “moderate,” or “strong”?

Have the mechanistic events been established? Are there consistent results in different experimental systems? Is the overall database coherent?

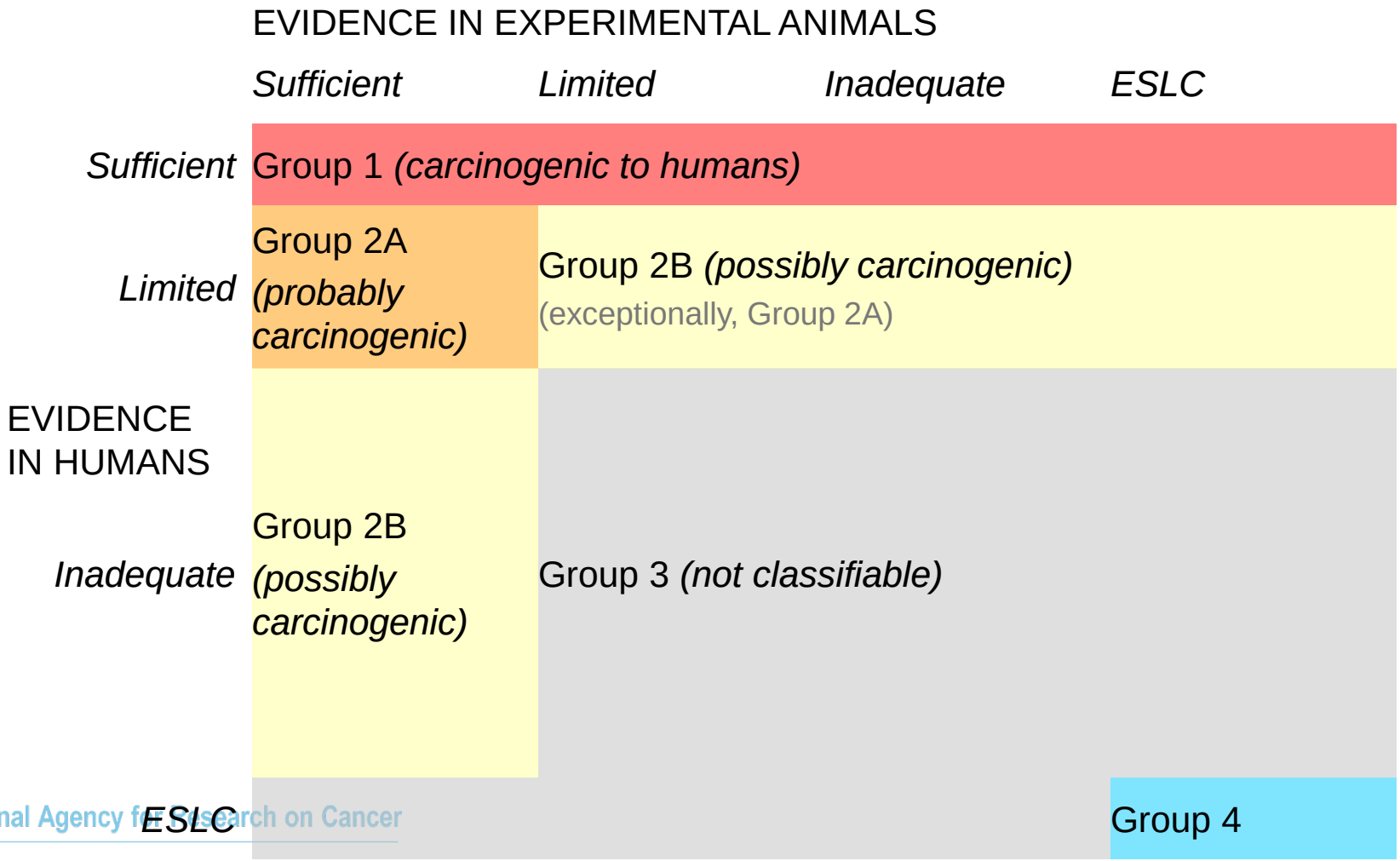
Has each mechanism been challenged experimentally? Do studies demonstrate that suppression of key mechanistic processes leads to suppression of tumour development?

- Is the mechanism likely to be operative in humans?

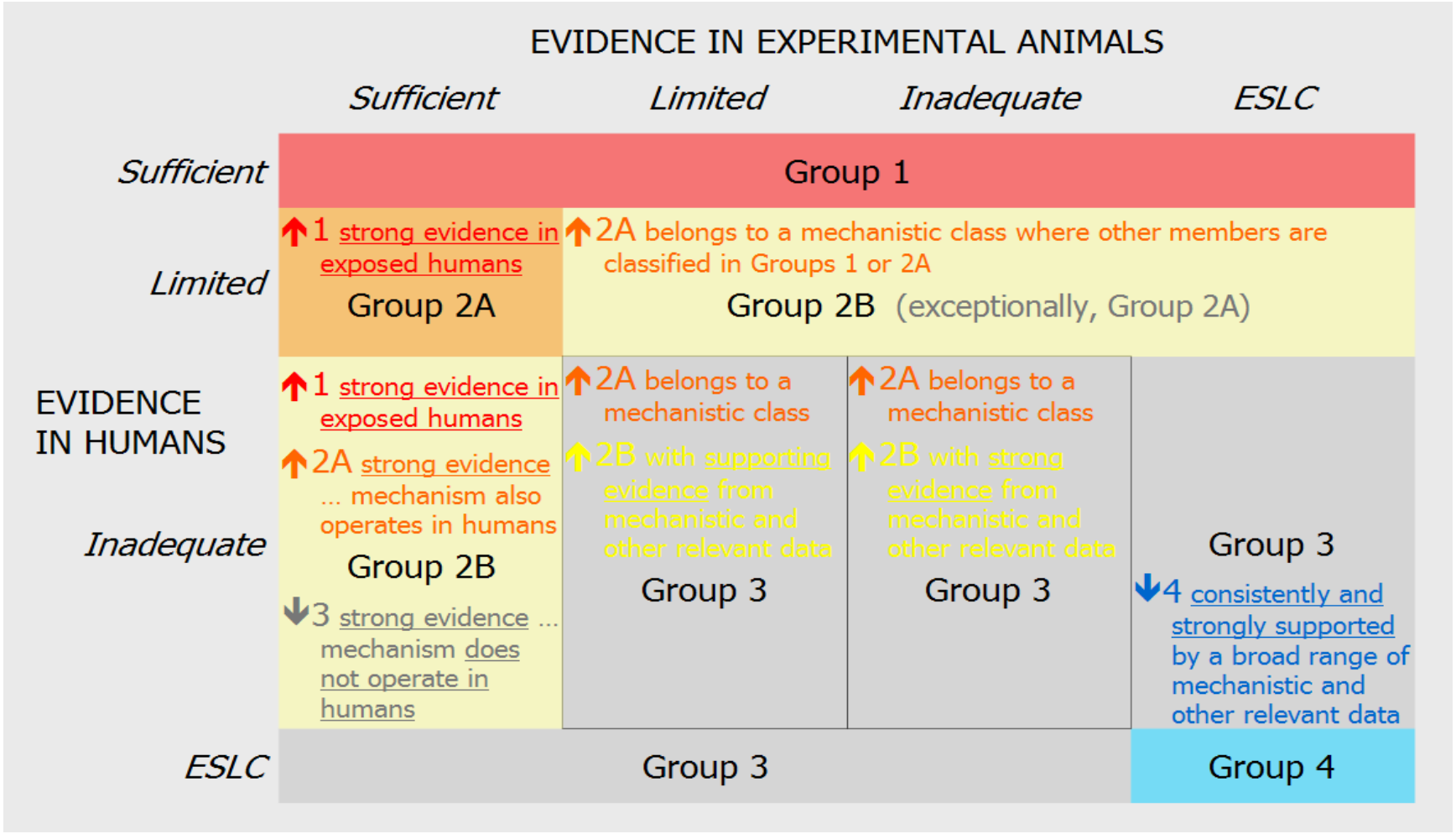
Are there alternative explanations? Could different mechanisms operate in different dose ranges, in humans and experimental animals, or in a susceptible group?

Note: an uneven level of support for different mechanisms may reflect only the resources focused on each one

The plenary sessions will combine the human and experimental evaluations

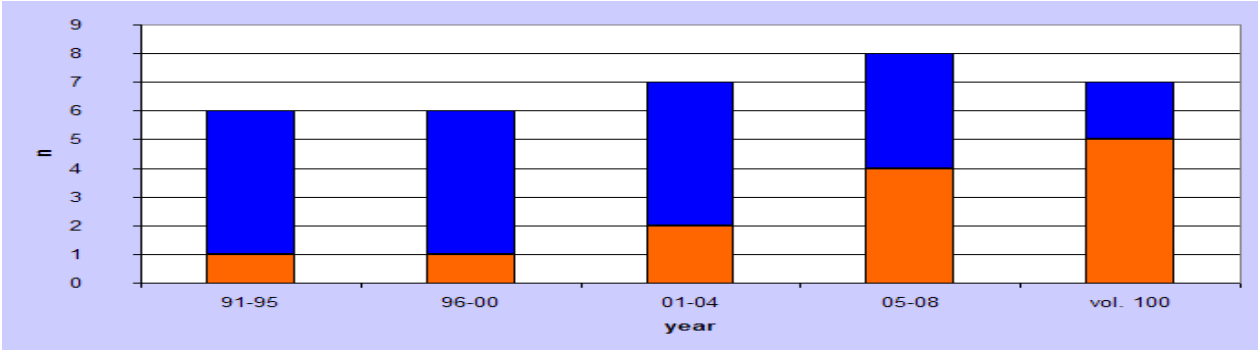


Overall carcinogenicity evaluation



Mechanisms Involved in Human Carcinogenesis

Use of mechanistic data to identify carcinogens is accelerating



Total new Group 1

Mechanistic up-grades to Group 1

Types of mechanistic upgrades

Ethylene oxide: Dose-related increase in the frequency of SCE, CA, and MN in lymphocytes of exposed workers.

Benzo[a]pyrene: Genotoxic mechanism involves its metabolism to highly reactive species that form covalent adducts to DNA that induce mutations in K-Ras and the TP53 genes in both human and mouse lung tumours. K-RAS mutations have been found in nonsmokers exposed to coal smoke

Benzidine-based dyes: Metabolism results in the release of free benzidine in humans and in all experimental animal species studied.

IARC Monographs, Volume 100
A Review of Human Carcinogens

- Scope of volume 100
  - Update the critical review for each carcinogen in Group 1
  - Identify tumour sites and plausible mechanisms
  - Compile information for subsequent scientific publications
- The volume was developed over the course of 6 meetings
  A. *Pharmaceuticals* (23 agents, Oct 2008)
  B. *Biological agents* (11 agents, Feb 2009)
  C. Metals, particles and fibres (14 agents, Mar 2009)
  D. Radiation (14 agents, June 2009)
  E. Lifestyle factors (11 agents, Sept 2009)
  F. Chemicals and related occupations (34 agents, Oct 2009)

International Agency for Research on Cancer

World Health Organization

Preventable Exposures Associated With Human Cancers

Vincent James Cogliano, Robert Baan, Kurt Straif, Yann Grosse, Béatrice Lauby-Secretan, Fatiha El Ghissassi, Véronique Bouvard, Lamia Benbrahim-Tallaa, Neela Guha, Crystal Freeman, Laurent Galichet, Christopher P. Wild

Known and suspected causes of cancer

List of Classifications by cancer sites with *sufficient* or *limited evidence* in humans, Volumes 1 to 108*

Cancer site	Carcinogenic agents with *sufficient evidence* in humans	Agents with *limited evidence* in humans
Lung	Aluminum production Arsenic and inorganic arsenic compounds Asbestos (all forms) Beryllium and beryllium compounds Bis(chloromethyl)ether; chloromethyl methyl ether (technical grade) Cadmium and cadmium compounds Chromium(VI) compounds Coal, indoor emissions from household combustion Coal gasification Coal-tar pitch Coke production Engine exhaust, diesel	Acid mists, strong inorganic Art glass, glass containers and pressed ware (manufacture of) Biomass fuel (primarily wood), indoor emissions from household combustion of Bitumens, occupational exposure to oxidized bitumens and their emissions during roofing Bitumens, occupational exposure to hard bitumens and their emissions during mastic asphalt work Carbon electrode manufacture

Boot & shoe manufacturing & repair, Vol 25, and Suppl 7

- Employment in the boot and shoe industry is causally associated with the development of nasal adenocarcinomas; and relative risks well in excess of 10-fold have been reported in England and in Italy.
- It is most likely that exposure to leather dust plays a role in the association. There is also evidence that an increased risk may exist for other types of nasal cancers for employment in boot and shoe repairing shops.
- The occurrence of leukaemia and aplastic anaemia among shoemakers exposed to benzene is well documented (see also IARC, Vol 7, 1974)

Boot & shoe manufacturing & repair, Leather dust, Vol 100F

- Consistent and strong evidence from descriptive and case-control studies for increased risk of sinonasal cancer in the boot and shoe industry.
- Very large excess risks particularly for sino-nasal adenocarcinoma.
- Excess highest among workers with leather dust exposure.

Evaluation

- There is sufficient evidence in humans for the carcinogenicity of leather dust. Leather dust causes sinonasal cancer.
- There are no data in experimental animals for the carcinogenicity of leather dust.

Overall evaluation

- Leather dust is carcinogenic to humans (Group 1).

Occupational exposure as a Painter (Vol 98)

Cancer in humans

There is *sufficient evidence* in humans for the carcinogenicity of occupational exposure as a painter.

- Occupational exposure as a painter causes cancers of the lung and urinary bladder.
- There is *limited evidence* in humans, based primarily on studies of maternal exposure, that painting is associated with childhood leukaemia.

Overall evaluation

Occupational exposure as a painter is *carcinogenic to humans (Group 1)*.

Classification of occupations

- Some occupations classified as carcinogenic to humans have had subsequent reviews attribute their carcinogenicity to specific chemical or physical agents.
- Examples are boot and shoe manufacture and repair (respiratory tract cancers are now attributed to leather dust; and leukemia, to benzene),
- These and other occupations should be regarded as carcinogenic to humans whenever there is exposure to the carcinogenic agents identified in those workplaces.
- Attributing carcinogenicity to specific agents helps national agencies develop regulations to prevent exposure to these agents wherever they are found, in the workplace or in the general environment

REVIEW

Preventable Exposures Associated With Human Cancers

Vincent James Cogliano, Robert Baan, Kurt Straif, Yann Grosse, Béatrice Lauby-Secretan, Fatiha El Ghissassi, Véronique Bouvard, Lamia Benbrahim-Tallaa, Neela Guha, Crystal Freeman, Laurent Galichet, Christopher P. Wild

Occupational exposure as a Firefighter (Vol 98)

Exposure

- Several types of firefighters exist, including municipal, wildland, industrial, aviation, and military firefighters.
- All fires generate an enormous number of toxic combustion products, including known and possible carcinogens, long-lived free radicals, and particulate matter. Smoke particles may serve as vehicles for adsorbed volatile organic compounds.

Occupational exposure as a Firefighter (Vol 98)

Exposure

- Peak exposures to some carcinogens may be very high, notably for benzene, 1,3-butadiene, and formaldehyde.
- The concentrations of respirable particulate matter to which firefighters may be exposed during overhaul can reach 50 mg/m3, or up to 1000 mg/m3, and above in the case of coarser particles.

Occupational exposure as a Firefighter (Vol 98)

Cancer in humans (I)

The Working Group reviewed

- 42 studies of cancer in firefighters that included
  19 cohorts,
  11 case–control studies, and
  14 studies that used other designs.
- The studies that were most relevant to the assessment of the risk for cancer among firefighters were the larger historical cohort studies.

Occupational exposure as a Firefighter (Vol 98)

Cancer in humans (II)

- Although excesses of a variety of cancers have been observed in several studies, consistent patterns are difficult to discern due to the large variations of exposures.
- For intermittent but intense exposures to highly variable complex mixtures conventional measures such as years of employment or number of firefighting runs may be poor surrogates for exposure.
- The available epidemiological studies are inherently limited by this.

Occupational exposure as a Firefighter (Vol 98)

Cancer in humans (III)

- The Working Group up-dated a recent meta-analysis of cancer in firefighters (LeMasters et al, 2006).
- For 3 types of cancer the RR were consistently increased and the average increase was statistically significant:
- Testicular cancer (all 6 studies showed increased risks, average relative risk 1.5), 1/3 with trend with duration
- Prostate cancer (increased risks in 18 of 21 studies, average relative risk 1.3), and
- non-Hodgkin lymphoma (increased risks in 5 of 6 studies, average relative risk 1.2).

Occupational exposure as a Firefighter (Vol 98)

Mechanisms of carcinogenicity

- The toxicokinetics of chemical mixtures are not well understood but are probably of significant importance because of the multiplicity of chemicals in smoke.
- For individual smoke components, inhalation was considered to be the major source of exposure; however, dermal absorption is also an important route of exposure for polycyclic aromatic hydrocarbons and polychlorinated biphenyls.

Occupational exposure as a Firefighter (Vol 98)

Mechanisms of carcinogenicity

- Studies to evaluate genotoxic effects in firefighters are few and not conclusive.
- Acute and chronic inflammatory respiratory effects observed in firefighters (Burgess et al, 1999) would provide a plausible mechanism for respiratory carcinogenesis.

Occupational exposure as a Firefighter (Vol 98)

Evaluation, Cancer in humans

- There is *limited evidence* in humans that occupation as a firefighter is carcinogenic.
- There is some evidence for an increased risk of testicular cancer, non-Hodgkin lymphoma and prostate cancer

Overall evaluation

- Occupation as a firefighter is *possibly carcinogenic to humans (Group 2B).*

IARC Workshop: Defining 'Shift Work' for epidemiological Studies of Cancer

Working time	Workhours/week
Night work	At least 3 hrs of work between midnight and 5 am
Duration	Years employed in non-day shift work
Intensity	Number of non-day shifts per month/year
Cumulative exp.	Duration times intensity over the work history
Permanent shift	# consecutive days of night work, followed by # days off
Rotating type	Continuous (365 days/year) or dis-continuous
Direction of rotation	Forward (morning → afternoon/evening → night) backward (afternoon/evening → morning → night)
Rate of rotation	Daily change, 2-3-4 day change, weekly, etc.
Morning shift	# consecutive days of early morning shift (before 6 am)
Start/end time	Displacement from solar day, duration of the working hours
Rest after shift	Number of rest-days after night shifts
Jetlag	No of time zones crossed; eastward vs. westward
Sleep	Sleep duration &
Light at night	During sleep peri
Characteristics of the individual	Diurnal type (mor

World Health Organization

Considerations of circadian impact for defining 'shift work' in cancer studies: IARC Working Group Report

Richard G Stevens,[1] Johnni Hansen,[2] Giovanni Costa,[3] Erhard Haus,[4] Timo Kauppinen,[5] Kristan J Aronson,[6] Gemma Castaño-Vinyals,[7] Scott Davis,[8] Monique H W Frings-Dresen,[9] Lin Fritschi,[10] Manolis Kogevinas,[11] Kazutaka Kogi,[12] Jenny-Anne Lie,[13] Arne Lowden,[14] Beata Peplonska,[15] Beate Pesch,[16] Eero Pukkala,[17] Eva Schernhammer,[18] Ruth C Travis,[19] Roel Vermeulen,[20] Tongzhang Zheng,[21] Vincent Cogliano,[22] Kurt Straif[22]

Joint IARC, NIOSH-NORA, ACS, US NIEHS and NCI Workshop

Review

Research Recommendations for Selected IARC-Classified Agents

Elizabeth M. Ward,[1] Paul A. Schulte,[2] Kurt Straif,[3] Nancy B. Hopf,[4] Jane C. Caldwell,[5] Tania Carreón,[2] David M. DeMarini,[5] Bruce A. Fowler,[6] Bernard D. Goldstein,[7] Kari Hemminki,[8] Cynthia J. Hines,[2] Kirsti Husgafvel Pursiainen,[9] Eileen Kuempel,[2] Joellen Lewtas,[10] Ruth M. Lunn,[11] Elsebeth Lynge,[12] Damien M. McElvenny,[13] Hartwig Muhle,[14] Tamie Nakajima,[15] Larry W. Robertson,[16] Nathaniel Rothman,[17] Avima M. Ruder,[2] Mary K. Schubauer-Berigan,[2] Jack Siemiatycki,[18] Debra Silverman,[17] Martyn T. Smith,[19] Tom Sorahan,[20] Kyle Steenland,[21] Richard G. Stevens,[22] Paolo Vineis,[23] Shelia Hoar Zahm,[17] Lauren Zeise,[24] and Vincent J. Cogliano[3]

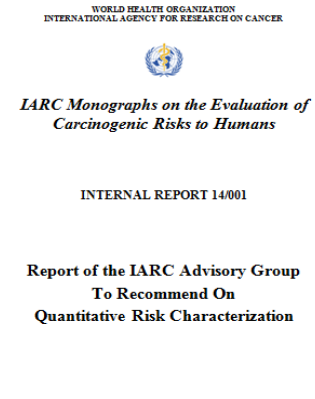
Acetaldehyde
Atrazine
Carbon black
Chloroform
Cobalt metal with tungsten carbide
Dichloromethane
Diesel engine exhaust
Di-2-ethylhexyl phthalate
Formaldehyde
Indium phosphide
Lead and lead compounds
Polychlorinated biphenyls (PCB)
Propylene oxide
Refractory ceramic fibers
Shiftwork that involves nightwork
Styrene
Tetrachloroethylene
Titanium dioxide
Trichloroethylene
Welding fumes

International Agency for Research on Cancer

World Health Organization

AG Quantitative Risk Characterization, Nov. 2013

- Suggestions for enhancements of the *Monographs* that would be likely to result in contributions to QRC
  - review cancer burden and other risk scenarios from the literature
  - summarize exposure–response relationships seen in epidemiological studies
  - should not formally review existing national risk assessments
- Additional resources will be needed to pursue QRC to the point of developing risk estimates, combining these risks with exposures and predicting cancer burden.


WORLD HEALTH ORGANIZATION
INTERNATIONAL AGENCY FOR RESEARCH ON CANCER

IARC Monographs on the Evaluation of Carcinogenic Risks to Humans

INTERNAL REPORT 14/001

Report of the IARC Advisory Group To Recommend On Quantitative Risk Characterization

18–19 November 2013

LYON, FRANCE
2014

International Agency for Research on Cancer

World Health Organization

Future priorities for the IARC Monographs

News

An Advisory Group of 21 scientists from 13 countries met in April, 2014, to recommend topics for assessment in 2015–19 and to discuss strategic matters for the International Agency for Research on Cancer (IARC) Monographs programme. IARC periodically convenes such advisory groups to ensure that the Monographs reflect the current state of priorities for public health.

The Advisory Group assessed the responses to a call for nominations on the IARC website and recommended a broad range of agents and exposures for assessment with high or medium

Lancet Oncol 2014
Published Online
May 6, 2014

Panel: Agents recommended by the IARC Advisory Group for assessment

High priority

Acrylamide, furan, and 5-(hydroxymethyl) furfural—commonly found in cooked foods; cancer bioassay data are available

Aspartame and sucralose—widespread use and concern about their potential carcinogenicity

- Beta-carotene
- Bisphenol A
- Disinfected water
- Dimethylformamide
- HCMV
- Indium-tin oxide
- Iron, dietary
- Coal mining
- MTBE, ETBE
- Nicotine
- Obesity , Physical inactivity
- Opium
- Phenyl and octyl tin compounds
- Pesticides
- Shift work
- Styrene
- Welding

International Agency for Research on Cancer

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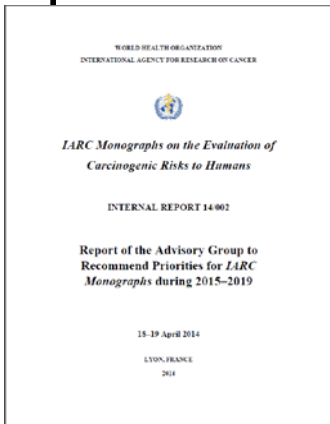
WORLD HEALTH ORGANIZATION
INTERNATIONAL AGENCY FOR RESEARCH ON CANCER

IARC Monographs on the Evaluation of Carcinogenic Risks to Humans

INTERNAL REPORT 14/002

Report of the Advisory Group to Recommend Priorities for *IARC Monographs* during 2015–2019

15–19 April 2014

LYON, FRANCE
2014

IARC MONOGRAPHS – MEETINGS

Upcoming Meetings

Meeting 114: Red Meat and Processed Meat
(6-13 October 2015)

Call for Data (closing date 11 September 2015)
Call for Experts (closing date 6 February 2015)
Request for Observer Status (closing date 5 June 2015)
WHO Declaration of Interests for this volume
Instructions for Authors

Meeting 115: Some Industrial Chemicals
(2-9 February 2016)

Preliminary List of Agents
Call for Data (closing date 4 January 2016)
Call for Experts (closing date 1 June 2015)
Request for Observer Status (closing date 5 October 2015)
WHO Declaration of Interests for this volume
Instructions for Authors

Meeting 116: Coffee and Some Other Hot Beverages
(24-31 May 2016)

International Agency for Research on Cancer

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Call for nominations of agents for review in future *IARC Monographs*

IARC encourages the general public, the scientific community, national health agencies, and other organizations, to nominate agents for review in future *IARC Monographs*. For details, please see:
Information on nominations

Acknowledgements

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- **U.S. National Cancer Institute (since 1982)**
- **European Commission, DG Employment, Social Affairs and Inclusion (since 1986)**
- **U.S. National Institute of Environmental Health Sciences (since 1992)**
- **Institut National du Cancer (INCa), France**
- **U.S. Center for Disease Control (CDC)**

International Agency for Research on Cancer

World Health Organization

Danke !