

## Carcinogens in Tobacco Smoke

Tobacco smoke is a noxious mixture of thousands of constituents, several of which are carcinogenic. Based on current knowledge, 90 carcinogens are compiled using the evaluation of the following agencies:

1. The worldwide recognized, International Agency for Research on Cancer (IARC), part of the World Health Organization, which publishes a series of Monographs on the Evaluation of Carcinogenic Risks to Humans, based on evaluation of carcinogenicity of agents by a Working Group of experts.
2. The German Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area (MAK Commission) of the Deutsche Forschungsgemeinschaft (DFG) which annually evaluates substances for their toxicity and carcinogenicity.

Carcinogens can cause cancer through genotoxic or nongenotoxic mechanisms. Genotoxic carcinogens are either direct acting or require metabolic activation in the body to form ultimate carcinogens. Carcinogens can damage DNA by covalently modifying genomic DNA to form carcinogen-DNA adducts. DNA repair enzymes efficiently remove most damage. However, if a cell with DNA damage is not repaired or eliminated by apoptosis (programmed cell death), heritable alteration or mutation can occur during replication resulting in somatic gene mutation. As cancer is attributable to mutations, the repeated carcinogenic stimuli such as cigarette smoke are likely to overwhelm defensive processes like DNA repair or apoptosis.

The list of tobacco smoke carcinogens is not exhaustive as probably more constituents will be evaluated and found to have a carcinogenic/co-carcinogenic potential in the future.

The following table lists 90 carcinogens in cigarette smoke based on evaluation by IARC or DFG categorization as briefly defined below:

**IARC:** Group 1: The agent (mixture) is definitely carcinogenic to humans. The exposure circumstance entails exposures that are carcinogenic to humans. Group 2A: The agent (mixture) is probably carcinogenic to humans. The exposure circumstance entails exposures that are probably carcinogenic to humans. Group 2B: The agent (mixture) is possibly carcinogenic to humans. The exposure circumstance entails exposures that are possibly carcinogenic to humans.

**DFG:** Category 1: Cause cancer in man and can be assumed to make a significant contribution to cancer risk. Category 2:

Considered to be carcinogenic for man because sufficient data from long-term animal studies or limited evidence from animal studies substantiated by evidence from epidemiological studies indicate that they can make a significant contribution to cancer risk. Category 3: Cause concern that they could be carcinogenic for man but cannot be assessed conclusively because of lack of data. The classification in Category 3 is provisional. 3A: The criteria for classification in Category 4 or 5 are fulfilled but for which the database is insufficient for the establishment of a MAK or BAT value. 3B: In vitro or animal studies have yielded evidence of carcinogenic effects (...).

### References

- (1) Deutsche Forschungsgemeinschaft (2008) List of MAK and BAT values 2008, commission for the investigation of health hazards of chemical compounds in the work area, Report No. 44. Wiley-VCH, Weinheim
- (2) International Agency for Research on Cancer (2008) IARC Monographs Volumes 1-99, overall evaluations of carcinogenicity to humans, last update 28.04.08. <http://monographs.iarc.fr/ENG/Classification/crthallist.php> (downloaded 04.25.2009)

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## List of 90 agents in cigarette smoke that have been classified as carcinogenic or possibly carcinogenic by IARC or DFG

No.	Agent	Carcinogenicity evaluation IARC or DFG	No.	Agent	Carcinogenicity evaluation IARC or DFG
<b>Polycyclic aromatic hydrocarbons</b>			<b>Aldehydes</b>		
1	Benz[ <i>a</i> ]anthracene	2B	50	Formaldehyde	1
2	Benzo[ <i>b</i> ]fluoranthene	2B	51	Acetaldehyde	2B
3	Benzo[ <i>j</i> ]fluoranthene	2B	52	Glyoxal	3B (DFG)
4	Benzo[ <i>k</i> ]fluoranthene	2B	53	Acrolein (2-Propenal)	3B (DFG)
5	Benzo[ <i>a</i> ]pyrene	1	54	Crotonaldehyde ( <i>trans</i> -2-Butenal)	3B (DFG)
6	Dibenzo[ <i>a,h</i> ]anthracene	2A	55	Furfural (2-Furylmethanal)	3B (DFG)
7	Dibenzo[ <i>a,i</i> ]pyrene	2B	<b>Phenolic compounds</b>		
8	Dibenzo[ <i>a,e</i> ]pyrene	2 (DFG)	56	Phenol	3B (DFG)
9	Indeno[1,2,3- <i>cd</i> ]pyrene	2B	57	Catechol	2B
10	5-Methylchrysene	2B	58	Hydroquinone	2 (DFG)
11	Chrysene	2B	59	<i>o</i> -, <i>m</i> -, <i>p</i> -Cresol	3A (DFG)
12	Cyclopenta[ <i>cd</i> ]pyrene	2A	60	Caffeic acid	2B
13	Dibenzo[ <i>a,h</i> ]pyrene	2B	<b>Volatile Hydrocarbons</b>		
14	Dibenzo[ <i>a,l</i> ]pyrene	2A	61	1,3-Butadiene	1
15	Naphthalene	2B	62	Isoprene	2B
16	Anthanthrene	2 (DFG)	63	Benzene	1
17	1-Methylpyrene	2 (DFG)	64	Nitromethane	2B
18	Benzo[ <i>b</i> ]naphtho[2,1- <i>d</i> ]thiophene	2 (DFG)	65	2-Nitropropane	2B
19	<b>Heterocyclic hydrocarbons</b> Furan	2B	66	Nitrobenzene	2B
20	Dibenz[ <i>a,h</i> ]acridine	2B	<b>Micellaneous organic compounds</b>		
21	Dibenz[ <i>a,i</i> ]acridine	2B	67	Acetamide	2B
22	Dibenzo[ <i>c,g</i> ]carbazole	2B	68	Acrylamide	2A
23	Benzo[ <i>b</i> ]furan	2B	69	Acrylonitrile	2B
24	<b><i>N</i>-Nitrosamines</b> <i>N</i> -Nitrosodimethylamine	2A	70	Vinyl acetate	2B
25	<i>N</i> -Nitrosomethylethylamine	2B	71	Vinyl chloride	1
26	<i>N</i> -Nitrosodiethylamine	2A	72	Hydrazine	2B
27	<i>N</i> -Nitrosodi- <i>n</i> -propylamine	2B	73	1,1-Dimethylhydrazine	2B
28	<i>N</i> -Nitrosodi- <i>n</i> -butylamine	2B	74	Ethylene oxide	1
29	<i>N</i> -Nitrosopyrrolidine	2B	75	Propylene oxide	2B
30	<i>N</i> -Nitrosopiperidine	2B	76	Styrene	2B
31	<i>N</i> -Nitrosodiethanolamine	2B	77	Safrol	2B
32	4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanone („NNK“) together with	} 1	78	Glycidol	2A
33	<i>N</i> -Nitrosornicotine („NNN“)		79	Urethane	2B
34	<b>Gas</b> Nitrogen dioxide NO <sub>2</sub>	3B(DFG)	80	1,1,1-trichlor-2,2-bis(4-chlorphenyl)-ethane	2B
35	<b>Aromatic amines</b> 2-Toluidine	1	81	Heptachlor	2B
36	4-Toluidine	3B (DFG)	<b>Metals and metal compounds</b>		
37	2,6-Dimethylaniline	2B	82	Arsenic	1
38	<i>o</i> -Anisidine	2B	83	Beryllium	1
39	2-Naphthylamine	1	84	Nickel	1
40	4-Aminobiphenyl	1	85	Chromium (hexavalent)	1
41	<b><i>N</i>-Heterocyclic amines</b> 2-Amino-9H-pyrido[2,3- <i>b</i> ]indole (A- $\alpha$ -C)	2B	86	Cadmium	1
42	2-Amino-3-methylimidazo-[4,5- <i>b</i> ]chinoline („IQ“)	2A	87	Cobalt	2B
43	2-Amino-3,4-dimethyl-3H-imidazo[4,5- <i>f</i> ]quinoline (MeIQ)	2B	88	Selenium	3B (DFG)
44	3-Amino-1,4-dimethyl-5H-pyrido[4,3- <i>b</i> ]indole („Trp-P-1“)	2B	89	Lead (inorganic)	2A
45	3-Amino-1-methyl-5H-pyrido[4,3- <i>b</i> ]indole („Trp-P-2“)	2B	<b>Radio-isotope</b>		
46	2-Amino-6-methyl[1,2- <i>a</i> : 3',2"- <i>d</i> ]imidazole („Glu-P-1“)	2B	90	Polonium-210	1
47	2-Aminodipyrido[1,2- <i>a</i> : 3',2"- <i>d</i> ]imidazole („Glu-P-2“)	2B			
48	2-Amino-1-methyl-6-phenylimidazo[4,5- <i>b</i> ]pyridine („PhIP“)	2B			
49	2-Amino-3-methyl-9H-pyrido[2,3- <i>b</i> ]indol (MeA- $\alpha$ -C)	2B			