



## FACTSHEET

# 11<sup>th</sup> Report on Carcinogens

## The Report on Carcinogens, Eleventh Edition

The Department of Health and Human Services released the Report on Carcinogens (RoC), Eleventh Edition on January 31, 2005. Prepared by the National Toxicology Program (NTP), the RoC identifies agents—such as metals, pesticides, drugs, viruses, ionizing radiation and natural and synthetic chemicals and mixtures or exposure circumstances that are “known” or are “reasonably anticipated” to cause cancer, and to which a significant number of Americans are exposed.

The RoC is a scientific and public health document first ordered by Congress in 1978 to educate both the public and health professionals in the recognition that many cancers are apparently induced by chemicals in the home, the workplace, the general environment and from the use of certain drugs. It is important to understand that the RoC identifies *potential* cancer hazards. A listing in the RoC does not by itself establish that a substance presents a cancer risk to an individual in daily life. It is also important to note that the RoC does not address or attempt to balance potential benefits of exposures to certain carcinogenic substances in special situations. For example, numerous anti-cancer drugs have been shown to increase the occurrence of secondary cancers. In these instances, the benefits of exposure to the drugs for treatment or prevention of a specific disease outweigh the additional cancer risks associated with their use. People should not make decisions concerning the use of a given drug, or any other listed agent, based solely on the information contained in the RoC. Decisions of this type should be made only after consulting with a physician or other appropriate specialist about both risks and benefits.

### Listing Categories

An agent, substance, mixture or exposure circumstance can be listed in the RoC either as “known to be a human carcinogen” or as “reasonably anticipated to be a human carcinogen.”

The “known” category is reserved for those substances for which sufficient evidence of carcinogenicity from studies in humans exists indicating a cause and effect relationship between exposure to the substance and human cancer.

The “reasonably anticipated” category includes those substances for which there is limited evidence of carcinogenicity in humans and/or sufficient evidence of carcinogenicity in experimental animals indicating a cause and effect relationship between exposure to the substance and cancer.

Conclusions regarding carcinogenicity in humans or experimental animals are based on expert, scientific judgment, with consideration given to all relevant information.

### Listings in the Report on Carcinogens, Eleventh Edition

The Eleventh Edition of the RoC contains 246 entries, 58 of which are listed as *known to be human carcinogens* and with the remaining 188 being listed as *reasonably anticipated to be human carcinogens*. Seventeen of the listings are new to the report.

The new listings in the Eleventh Edition include lead and lead compounds, x- and gamma ( $\gamma$ )-radiation, compounds found in grilled meats, and a host of substances used in textile dyes, paints and inks. The report also includes the listing of viruses for the first time including some human papillomaviruses, which causes one of the most common sexually transmitted disease, and Hepatitis B and C viruses. The RoC’s findings are based

on three years of review and evaluation that included three independent scientific reviews and public comment from scientists, consumers and other interested parties.

The listing of a substance in the RoC is not a regulatory action, but listing may prompt regulatory agencies to consider limiting exposures or uses of a substance. In addition, the U.S. Congress, federal and state agencies, businesses, unions and the general public all use the RoC as an authoritative source concerning human cancer hazards.

**The following briefly describes the additions  
and/or changes made in the Eleventh Edition of the RoC:**

**Added as “known human carcinogens” in the Eleventh Edition of the RoC:**

***Hepatitis B Virus (HBV)***—Hepatitis B Virus is listed in the Eleventh Edition of the RoC as a “known human carcinogen.” HBV is an enveloped DNA virus that infects liver cells causing acute or chronic hepatitis B. In the United States, most cases result from heterosexual transmission (41%), intravenous drug use (15%), and homosexual transmission (9%); however, 31% of HBV infections are not associated with any known risk factors. In areas where HBV infection is endemic, an important route of transmission is from mother to infant. Over one million US residents are chronically infected with hepatitis B virus. The risk of chronic hepatitis B infection among HBV-infected individuals appears to depend on the status of the immune system at the time of infection and is much higher in HBV-infected infants and children than in HBV-infected adults. The prevalence rate of chronic hepatitis B infection in the United States is about 5% and declining slightly. HBV infections can be prevented by screening of the blood supply, reduction of contact with potentially contaminated fluids in health-care settings, and vaccination. The RoC listing is based on numerous cohort and case-control (epidemiological) studies conducted in populations differing by race or ethnicity and in various geographic regions, which have demonstrated that chronic HBV infection causes liver cancer.

***Hepatitis C Virus (HCV)***—Hepatitis C Virus is listed in the Eleventh Edition of the RoC as a “known human carcinogen”. HCV is an enveloped RNA virus, which causes acute or chronic hepatitis and is the leading cause of liver disease in the United States. The major route of HCV transmission is through contaminated blood. The major risk factor for infection is illegal intravenous drug use, which accounts for 60% of acute HCV infections in adults. Since the screening of blood and blood products for HCV began in the 1990s, blood transfusion has accounted for only a small percentage of adult HCV cases (about 3%). Other routes of transmission include sexual, perinatal (from mother to infant at birth), and familial (at low rates), through health-care practices, including transmission by contaminated equipment or supplies, from patient to patient (at low rates), and through occupational exposure (at low rates). In the United States, approximately 3 to 4 million people are infected with HCV. However, the annual number of newly acquired HCV infections declined from 180,000 in the mid 1980s to 28,000 by 1995, probably as a result of testing of blood donors and decreased numbers of cases among intravenous drug users. HCV infections can be prevented by screening of the blood supply and reduction of contact with potentially contaminated fluids in health-care settings. The RoC listing is based on numerous cohort and case-control (epidemiological) studies conducted in populations differing by race or ethnicity and in various geographical locations, which have demonstrated that chronic HCV infection causes liver cancer. There is some evidence to suggest that chronic HCV infection may increase the risk of B-cell lymphoma.

***Human Papillomaviruses (HPVs), Some Genital-Mucosal Types***—Some human papillomaviruses of the genital-mucosal type are listed in the Eleventh Edition of the RoC as “known human carcinogens.” HPVs of the genital-mucosal type are DNA viruses that infect the genital skin and genital and non-genital mucosa and sometimes cause genital warts or cervical abnormalities although most infected people do not have symptoms. HPV infection is one of the most common sexually transmitted diseases and is transmitted through sexual contact with infected cervical, vaginal, vulvar, penile or anal epithelium. Approximately 20 million people in the United States are infected with HPV with 5.5 million new infections occurring each year. Treatment of HPV infection depends on the severity of the disease and may involve topical applications, interferon-related therapies, or excision of the lesion via laser methods, surgery, or cryotherapy. The RoC listing is based on epidemiological studies that have shown that some genital-mucosal HPVs cause cervical cancer. Case-control studies have reported strong associations with HPVs types 16, 18, 31, 33, 35, 39, 45, 51, 52, 58,59 and “high risk” HPVs as a class (the group of HPV viruses that have been shown to increase cancer risk in epidemiological studies) and cervical cancer. Cohort studies have demonstrated

that infection with HPV-16 or with high-risk HPVs as a class occurs before the development of high-grade cervical intraepithelial neoplasia (CIN), which is thought to be a precursor of invasive cancer. HPV-16 has also been associated with other anogenital cancers, especially cancer of the vulva.

**Three types of ionizing radiation: X-radiation, gamma-radiation, and neutrons**—X-radiation, gamma radiation, and neutrons are listed in the Eleventh Edition of the RoC as “known human carcinogens”. X-rays, gamma rays, and materials and processes that emit X-rays and gamma rays are used in medicine, the nuclear power industry, the military, scientific research, industry, and various consumer products. Neutron radiation is used less than other types of radiation in industry, medicine, and research. The most important sources of X-radiation and gamma radiation include natural sources, medical uses, atmospheric nuclear weapons tests, nuclear accidents, and nuclear power generation. Sources of neutron radiation include the interaction of high-energy cosmic rays with the earth’s atmosphere, nuclear fusion or fission of atomic nuclei in nuclear reactors or atomic explosions, and the collision of charged particles with a lithium or beryllium target. Of the estimated worldwide exposure to X-radiation and gamma radiation, about 43% is from natural sources, about 55% is from medical diagnosis and treatment with all other sources contributing less than 2%. The general population is exposed to neutrons primarily from cosmic radiation originating from outer space. The RoC listing for X-radiation and gamma radiation is based on sufficient evidence of carcinogenicity in humans and the RoC listing for neutrons is based on studies of their mechanisms of carcinogenesis. X-radiation and gamma radiation are most strongly associated with leukemia and cancer of the thyroid, breast, and lung. The risk of developing these cancers, however, depends to some extent on age at exposure with childhood exposure mainly responsible for increased leukemia and thyroid-cancer risks, reproductive-age exposure for increased breast cancer risk and exposure later in life to lung cancer risk. Associations between radiation exposure and cancer of the salivary glands, stomach, colon, bladder, ovary, central nervous system, and skin also have been reported. Neutrons cause genetic damage similar to that caused by X-radiation and gamma radiation, and they also produce gamma radiation when they interact with biological materials and thus would cause the same cancers as X-radiation and gamma radiation.

**Added as “reasonably anticipated to be human carcinogens” in the Eleventh Edition of the RoC:**

**1-Amino-2,4-dibromoanthraquinone** — 1-Amino-2,4-dibromoanthraquinone is listed in the Eleventh Edition of the RoC as “reasonably anticipated to be a human carcinogen”. It is an anthraquinone-derived vat dye that is used in the textile industry. The RoC listing is based on findings from oral studies of 1-amino-2,4-dibromoanthraquinone in multiple species of experimental animals that produced cancer at multiple tissue sites including liver, large intestine, kidney, and urinary bladder in rats and liver, forestomach and lung in mice. No human epidemiological studies have been reported that evaluated cancer risk specifically associated with exposure to 1-amino-2,4-dibromoanthraquinone; however, several studies have reported an excess of cancer among anthraquinone dye workers.

**Cobalt Sulfate**—Cobalt Sulfate is listed in the Eleventh Edition of the RoC as “reasonably anticipated to be a human carcinogen.” It is used in the electroplating and electrochemical industries; as a coloring agent for ceramics; as a drying agent in inks, paints, varnishes and linoleum, and has been added to animal feed as a mineral supplement. The RoC listing is based on findings from long-term inhalation studies of this chemical in laboratory animals where it caused lung tumors in both mice and rats and adrenal-gland tumors in female rats .

**Diazoaminobenzene**—Diazoaminobenzene is listed in the Eleventh Edition of the RoC as “reasonably anticipated to be a human carcinogen.” It is used as an intermediate in the production of dyes and to promote adhesion of natural rubber to steel. The RoC listing of diazoaminobenzene is based on evidence from studies in animals and with human tissue demonstrating that diazoaminobenzene is metabolized to benzene, a “known human carcinogen”, and on evidence that diazoaminobenzene causes genetic damage.

**Selected Heterocyclic Amines (three):**

- **2-Amino-3,4-dimethylimidazo[4,5-f]quinoline (MeIQ)**
- **2-Amino-3,8-dimethylimidazo[4,5-f]quinoxaline (MeIQx)**
- **2-Amino-1-methyl-6-phenylimidazo[4,5-b]pyridine (PhIP)**—MeIQ, MeIQx and PhIP are listed in the Eleventh Edition of the RoC as “reasonably anticipated to be human carcinogens.” They are part of a series of heterocyclic amines (HCAs) that are formed in food during heating or cooking at high temperatures and are

found in cooked meats and eggs and also in cigarette smoke. The RoC listing of these selected heterocyclic amines is based on findings from oral studies in multiple species of experimental animals that showed cancer in multiple organs including forestomach, cecum, colon, liver, oral cavity, Zymbal gland, mammary gland, and skin. Although evidence from human epidemiology suggests that consumption of well-done or grilled meat (which may contain these and/or other HCAs) may be associated with increased cancer risk in humans, the data are insufficient to support the conclusion that this risk is due specifically to MeIQx, MeIQ or PhIP present in these foods.

**Lead and Lead Compounds**—Lead and Lead Compounds are listed in the Eleventh Edition of the RoC as “reasonably anticipated to be human carcinogens.” Lead is used for making lead-acid storage batteries, ammunition and cable covering. Lead compounds are used in paint, glass, and ceramics; as fuel additives; and some traditional cosmetics. The RoC listing is based on limited evidence from studies in humans and sufficient evidence from studies in experimental animals. Lead exposure has been associated with small increases in risk for cancer of the lung or stomach in diverse human populations; however this evidence must be weighed against the potential for confounding by co-exposures such as smoking, arsenic, or diet. In studies with laboratory animals, lead compounds caused cancer of the kidney, brain or lung by multiple routes of exposure including oral and injection. Lead compounds have also been shown to cause cancer in the offspring of laboratory animals after exposure via the placenta or lactation.

**Naphthalene**—Naphthalene is listed in the Eleventh Edition of the RoC as “reasonably anticipated to be a human carcinogen.” Naphthalene is used as an intermediate in the synthesis of many industrial chemicals, and has been used as an ingredient in some moth repellants and toilet bowl deodorants. The RoC listing is based on sufficient evidence from studies in experimental animals. When administered by inhalation, naphthalene caused a highly malignant and extremely rare tumor of the lining of the nose as well as an uncommon respiratory nasal tumor in rats and a significant increase in benign lung tumors in female mice.

**Nitrobenzene**—Nitrobenzene is listed in the Eleventh Edition of the RoC as “reasonably anticipated to be a human carcinogen.” Nitrobenzene is used mainly in the production of aniline, itself a major chemical intermediate in the production of dyes. The RoC listing is based on sufficient evidence of carcinogenicity in experimental animals. When administered by inhalation, nitrobenzene caused significantly increased incidences of tumors of the liver, lung, thyroid and mammary gland in mice and of the liver, kidney and uterus in rats.

**Nitromethane**—Nitromethane is listed in the Eleventh Edition of the RoC as “reasonably anticipated to be a human carcinogen.” It is used in specialized fuels, in explosives and in the synthesis of nitromethane derivatives, pharmaceuticals, agricultural soil fumigants and industrial antimicrobials. The RoC listing is based on sufficient evidence of carcinogenicity in experimental animals. When administered by inhalation, nitromethane significantly increased the combined incidences of benign and malignant tumors of the liver, lung and in mice and mammary gland in female rats.

**4,4'-Thiodianiline**—4,4'-Thiodianiline is listed in the Eleventh Edition of the RoC as “reasonably anticipated to be a human carcinogen.” 4,4'-Thiodianiline has been used as an intermediate in the preparation of several diazo dyes. The RoC listing is based on sufficient evidence of carcinogenicity in experimental animals. Dietary exposure to thiodianiline significantly increased the incidence of tumors of the thyroid, liver, ear canal and uterus in mice and/or rats.

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The Eleventh Edition of the RoC is immediately accessible at <http://ntp.niehs.nih.gov> (select Report on Carcinogens). Questions concerning the Eleventh Edition of the RoC should be directed to:

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