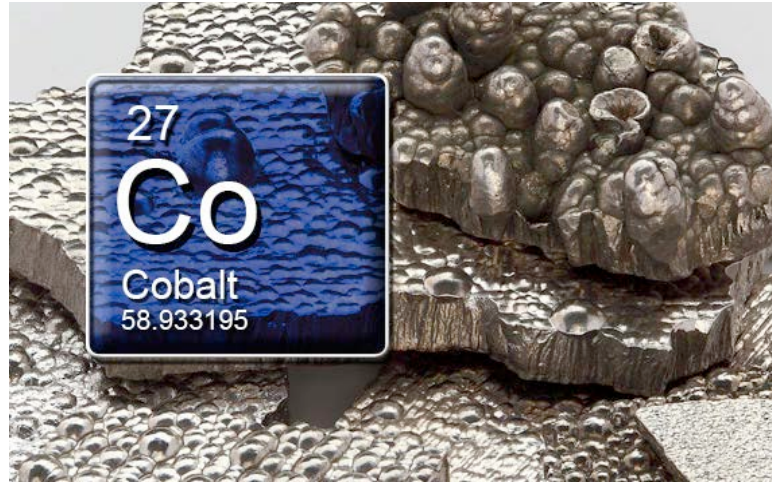


Cancer Evaluation Recommendation



Diane L. Spencer, MS

Office of the Report on Carcinogens

National Institute of Environmental Health Sciences

July 22, 2015



Exposure to cobalt causes carcinogenic effects in experimental animals

Site	Water soluble ($\text{CoSO}_4 \cdot 7\text{H}_2\text{O}$; CoCl_2)	Cobalt metal	Poorly water soluble (CoO)
Lung	Rat ♂♀ Mouse ♂♀	Rat ♂♀ Mouse ♂♀	Rat ♂
Pancreas		Rat ♂(♀)	
MCL		Rat ♀	
Kidney		Rat (♂)	
Adrenal gland	Rat ♀	Rat ♂♀	
Injection site	Rat ♂	Rat ♂♀	Rat ♂♀

() = results equivocal

MCL = mononuclear-cell leukemia



NTP's Level of Evidence Conclusion (Vote)

Sufficient evidence for the carcinogenicity of “Cobalt and Certain Cobalt Compounds” from studies in experimental animals

- Increased incidence of malignant and/or combination of malignant and benign neoplasms
 - Several tissue sites by inhalation/intratracheal exposure (lung, pancreas, MCL, adrenal gland) in rats and mice, both sexes
 - Supporting evidence from injection studies
- Tumors were induced in rodents by different forms of cobalt
 - Cobalt metal/nanoparticles
 - Water soluble cobalt compounds (cobalt sulfate heptahydrate, cobalt chloride)
 - Poorly water soluble cobalt compounds (cobalt(II) oxide)





Overall Cancer Evaluation

- There is inadequate evidence of carcinogenicity from human cancer studies on cobalt and certain cobalt compounds.
- There is sufficient evidence for carcinogenicity from experimental animal studies on cobalt and certain cobalt compounds.
- There is supporting mechanistic data for the carcinogenicity of cobalt and certain cobalt compounds.





Preliminary listing recommendation (Vote)

Cobalt and certain cobalt compounds are *reasonably anticipated to be human carcinogens*

- Sufficient evidence from studies in experimental animals
- Supporting data from studies on mechanisms of carcinogenesis

“*Certain*” is defined as compounds that release cobalt ions *in vivo*, which mechanistic data indicate is a key event for cobalt-induced carcinogenicity.

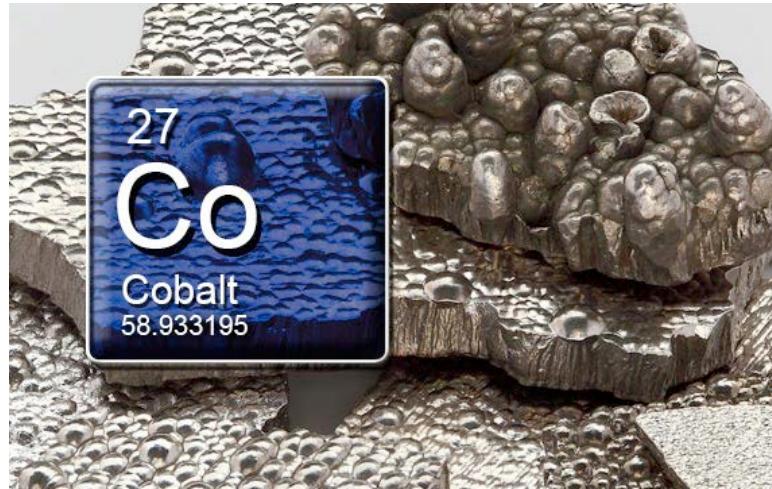




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Substance Profile



Diane L. Spencer, MS

Office of the Report on Carcinogens

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Contents of Substance Profile

- NTP's preliminary recommendation of the listing status of the substance
- Summary of scientific evidence key to reaching the recommendation
- Information on properties, use, production, and exposure
- Current federal regulations and guidelines to reduce exposure to the substance

N.B. Once the listing status is approved by the Secretary, HHS, the substance profile becomes a part of the next edition of the RoC.



Review of NTP's Preliminary Conclusions

- A significant number of people living in the United States are or have been exposed to cobalt and certain cobalt compounds.
- Data available from studies in humans are inadequate to evaluate the relationship between human cancer and exposure to cobalt and certain cobalt compounds.
- There is sufficient evidence of carcinogenicity for cobalt and certain cobalt compounds from studies in experimental animals.
- There is mechanistic evidence that supports the evidence for carcinogenicity in humans.
- There is a scientific rationale for listing cobalt and certain cobalt compounds as a group.



Reviewer Questions

- Comment on whether the information on use, production, and human exposure for cobalt and certain cobalt compounds is clear and technically accurate.
- Comment on whether the information presented regarding cancer studies in humans is clear, technically correct, and objectively stated.
 - Comment on whether the substance profile highlights the information from the cancer studies in humans that are considered key to reaching the listing recommendation.
- Comment on whether the information presented regarding cancer studies in experimental animals is clear, technically correct, and objectively stated.
 - Comment on whether the substance profile highlights the key information from the cancer studies in experimental animals that supports the listing recommendation.
- Comment on whether the information presented regarding studies on mechanisms of carcinogenicity and other relevant data is clear, technically correct, and objectively stated.
 - Comment on whether the substance profile highlights the studies on mechanisms of carcinogenicity and other relevant data that are key to providing support for the carcinogenicity of cobalt and certain cobalt compounds in humans.