



# Methods to Develop Inhalation Cancer Risk Estimates for Chromium and Nickel Compounds

# Methods to Develop Inhalation Cancer Risk Estimates for Chromium and Nickel Compounds

U.S. Environmental Protection Agency  
Office of Air Quality Planning and Standards  
Health and Environmental Impacts division  
Research Triangle Park, North Carolina

**Methods to Develop Inhalation Cancer Risk  
Estimates for Chromium and Nickel Compounds**

**Office of Air Quality Planning and Standards  
U.S. Environmental Protection Agency  
Research Triangle Park, NC 27711**

**October 2011**

## **Table of Contents**

1	Purpose .....	4
2	Chromium Compounds .....	4
2.1	Background .....	4
2.2	Approach for Estimating Inhalation Cancer Risks from Chromium Compounds.....	6
2.3	Approach for Developing Speciation Profiles for Selected Source Types .....	6
2.4	Chromium Speciation for Specific Source Types.....	7
2.4.1	Coal Boilers .....	7
2.4.2	Oil Boilers.....	7
2.5	Uncertainties and Limitations.....	8
2.6	Conclusions.....	9
3	Nickel and Compounds .....	10
3.1	Background .....	10
3.2	Approach for Estimating Inhalation Cancer Risks from Nickel Compounds.....	12
3.3	Approach for Developing Speciation Profiles for Selected Source Types .....	13
3.3.1	A. Approach to Derive Unit Risk Estimates: Electric Utility Report to Congress 1998 .....	13
3.3.2	B. Approach to Derive Unit Risk Estimates: NATA 2000 .....	13
3.3.3	C. Approach to Derive Unit Risk Estimates: Alternatives Based on Speciation of Residual Oil Fly Ashes from Power Plants.....	14
3.4	Uncertainties and limitations .....	15

### **List of Acronyms/Abbreviations**

CDHS	California Department of Health Services
DHHS	Department of Health and Human Services
Cr (VI)	Hexavalent chromium, also denoted as (Cr <sup>+6</sup> )
Cr (III)	Trivalent chromium, also denoted as (Cr <sup>+3</sup> )
EGUs	Electric Utility Steam Generating Units
EPA	Environmental Protection Agency
IARC	International Agency for Research on Carcinogenicity
IRIS	Integrated Risk Information System
NATA	National Scale Air Toxics Assessment
NTP	National Toxicology Program
ROC	Report of the Carcinogens
RTR	Risk and Technology Review
TECQ	Texas Commission on Environmental Quality
UREs	Unit risk estimates
WHO	World Health Organization
XAFS	X-ray absorption fine structure
XRD	Spectroscopy and x-ray diffraction

## 1 Purpose

The purpose of this paper is to discuss the methods used to develop inhalation cancer risk estimates associated with emissions of chromium and nickel compounds from coal- and oil-fired electric utility steam generating units (EGUs) in support of EPA's recently proposed Air Toxics Rule.<sup>1</sup> The derivation of cancer risk estimates is based on the speciation data available from selected source types, and on the available unit risk estimates (UREs) reflecting the dose that corresponds to a specific level of cancer risk. This document includes discussions for both emissions of chromium (Section 2) and nickel (Section 3) compounds with regard to: (1) the methods and rationale used in previous analyses (where applicable), (2) the methods used in the recent analysis for the Air Toxics Rule (considering previous methods and currently available data), and (3) a discussion of the uncertainties and/or limitations of the methods used. In this document, we consider the emissions of chromium compounds from both coal- and oil-fired EGUs and the emissions of nickel compounds from oil-fired EGUs, since these are major contributors to inhalation cancer risk estimates from each these source types.

## 2 Chromium Compounds

### 2.1 Background

Chromium compounds occur in nature and are found primarily in the earth's crust. The largest source of chromium is the ore mineral chromite,  $\text{FeCr}_2\text{O}_4$  or  $\text{MgCr}_2\text{O}_4$ , where magnesium can substitute for iron.<sup>2</sup> Chromium can also be found in small concentrations in certain types of igneous rocks, coal, tar, asphalt, and crude oil. Chromium compounds oxidation valences vary from  $-2$  to  $+6$ , but only the  $0$ ,  $+2$ ,  $+3$  and  $+6$  valence states are common.<sup>3</sup> However, the hexavalent state ( $\text{Cr}^{+6}$ ), also denoted as  $\text{Cr (VI)}$ , rarely occurs naturally, and is usually produced from anthropogenic sources (US EPA 1984).<sup>4</sup> The

---

<sup>1</sup> US EPA, 2011. National Emission Standards for Hazardous Air Pollutants from Coal- and Oil-fired Electric Utility Steam Generating Units and Standards of Performance for Fossil-Fuel-Fired Electric Utility, Industrial-commercial-Institutional, and Small Industrial-Commercial-Institutional Steam Generating Units Rule. Available online at <http://www.epa.gov/ttn/atw/utility/utilitypg.html>.

<sup>2</sup> Guertin, Jacques, James A. Jacobs and Cynthia P. Avakian. Chromium (VI) Handbook. Independent Environmental Technical Evaluation Group (IETEG). CRC Press, 2005. ISBN 9781566706087

<sup>3</sup> Dayan AD and Paine AJ. Mechanisms of chromium toxicity, carcinogenicity and allergenicity: review of the literature from 1985 to 2000. *Hum and Experiment Toxicol* 2001, 20:439-451.

<sup>4</sup> US EPA, 1984. Health assessment document for chromium. Research Triangle Park, NC: Environmental Assessment and Criteria Office, U.S. Environmental Protection Agency. EPA600/883014F.

trivalent state ( $\text{Cr}^{+3}$ ), also denoted as Cr (III), and the Cr(VI) state are the first and second most stable, respectively, and thus the forms considered more important with regard to human health.<sup>5</sup>

Chromium compounds are used in a variety of industrial applications and operations. They are used in alloys, such as stainless steel; paint pigments; refractory bricks that line furnaces and kilns; wood preservatives; production and processing of insoluble salts; in leather tanning; as catalysts for halogenation, alkylation, and catalytic cracking of hydrocarbons; as fuel and propellant additives; and more.<sup>6</sup> Many of these applications use substances containing Cr(VI) compounds, including various chromates, dichromates, and chromic acid.<sup>7</sup> Disposal of chemicals containing chromium or burning fossil fuels can also release chromium to the air, soil and water. In addition, some industrial processes may produce chromium emissions, wherein the hexavalent state is favored in an oxidizing alkaline environment, and the trivalent state is favored in a reducing acidic environment.<sup>8</sup> However the exact distribution between the hexavalent and trivalent chromium states in the environment is unknown.

In its 1998 IRIS Toxicological Review, the US EPA classified Cr(VI), including its compounds, as “a known human carcinogen by the inhalation route of exposure” based on evidence from occupational epidemiological studies consistently indicating dose-dependent associations between chromium inhalation exposure and lung cancer, and on supporting evidence from animal inhalation studies (US EPA, 1998)<sup>9</sup>. Further support comes from a recent 2-year chronic bioassay conducted by the National Toxicology Program (NTP) concluding that Cr(VI) is carcinogenic when ingested in drinking water. With regard to trivalent chromium Cr(III), the 1998 IRIS Toxicological Review notes that while the evidence from the occupational database “could be used to suggest that total chromium is carcinogenic by inhalation, animal data support the human carcinogenicity data only on hexavalent chromium”. Thus, based on these considerations the EPA concluded that only Cr(VI) should be classified as a human carcinogen. Further support for hexavalent chromium being the carcinogenic species is provided by a more recent, well-conducted, epidemiological study by Gibb et al., (2000)<sup>10</sup> showing dose-dependent associations between exposure to hexavalent chromium and the development of lung cancer in workers. The International

---

<sup>5</sup> Dayan AD and Paine AJ. Mechanisms of chromium toxicity, carcinogenicity and allergenicity: review of the literature from 1985 to 2000. *Hum and Experiment Toxicol* 2001, 20:439-451.

<sup>6</sup> Guertin J, Jacobs JA and Cynthia PA, 2005. Chromium (VI) Handbook. Independent Environmental Technical Evaluation Group (IETEG). CRC Press. ISBN 9781566706087

<sup>7</sup> Agency for Toxic Substances and Disease Registry (ATSDR), 1993. Toxicological Fact Sheet for chromium. Available online at [www.nativeknowledge.org/db/files/tfacts7.htm](http://www.nativeknowledge.org/db/files/tfacts7.htm)

<sup>8</sup> Guertin, Jacques, James A. Jacobs and Cynthia P. Avakian. Chromium (VI) Handbook. Independent Environmental Technical Evaluation Group (IETEG). CRC Press, 2005. ISBN 9781566706087

<sup>9</sup> US EPA, 1998. Integrated Risk Information Service (IRIS) assessment for hexavalent chromium. Available at: <http://www.epa.gov/ncea/iris/subst/0144.htm>.

<sup>10</sup> Gibb HJ, PS Lees, et al. (2000). Lung Cancer Among Workers in Chromium Chemical Production. *American J Ind Med* 38(2): 115-26.

Agency for Research on Carcinogenicity, or IARC, concluded that there are sufficient evidence for the carcinogenicity of Cr(VI) compounds in humans based on the combined evidence from the epidemiological, animal and mechanistic data available. In agreement with the EPA, the IARC stated that compounds of chromium III are not classifiable as to their carcinogenicity.<sup>11</sup> Scientific views similar to those of EPA and IARC are reflected in the NTP's *12<sup>th</sup> Report of the Carcinogens* (ROC).<sup>12</sup>

Cr (VI) has an inhalation unit risk estimate (URE)<sup>13</sup> of 0.012 per  $\mu\text{g}/\text{m}^3$ , which means that inhaling Cr(VI) in air at an average concentration of 1  $\mu\text{g}/\text{m}^3$  daily for a lifetime poses an estimated increased risk of cancer of 12,000 in a million.<sup>14</sup> This inhalation cancer potency value is among the highest values of any of the hazardous air pollutants (HAPs) listed in the Clean Air Act.

## 2.2 Approach for Estimating Inhalation Cancer Risks from Chromium Compounds

Based on the information in the previous section, we estimate cancer risks due to the inhalation of all chromium compounds based on the exposure concentration of Cr(VI) alone. Thus:

$$\text{Risk} = \text{EC}_{\text{Cr}} * \text{MF}_{\text{Cr(VI)}} * \text{URE}_{\text{Cr(VI)}}$$

Where

$\text{EC}_{\text{Cr}}$  is chronic exposure concentration for the mixture of all chromium compounds,  $\text{MF}_{\text{Cr(VI)}}$  is the mass fraction of the inhaled mixture which is hexavalent chromium, and  $\text{URE}_{\text{Cr(VI)}}$  is the cancer unit risk estimate for hexavalent chromium.

## 2.3 Approach for Developing Speciation Profiles for Selected Source Types

As discussed above, the toxicity of chromium compounds is largely dependent on its oxidation state (i.e., Cr(VI) vs. Cr(III), primarily) which is an important factor in evaluating the health effects from

---

<sup>11</sup> International Agency for Research on Cancer (IARC), 1990. IARC monographs on the evaluation of carcinogenic risks to humans. Chromium, nickel and welding. Vol. 49. Lyons, France: International Agency for Research on Cancer, World Health Organization 49-256.

<sup>12</sup> National Toxicology Program (NTP), 2011. Report on carcinogens. 12<sup>th</sup> ed. Research Triangle Park, NC: US Department of Health and Human Services (DHHS), Public Health Service. Available online at <http://ntp.niehs.nih.gov/ntp/roc/twelfth/roc12.pdf>.

<sup>13</sup> The inhalation Unit Risk Estimate (URE) represents the upper-bound excess lifetime cancer risk estimated to result from continuous exposure to an agent at a concentration of 1  $\mu\text{g}/\text{m}^3$  in air.

<sup>14</sup> US EPA, 1998. Study of Hazardous Air Pollutant Emissions from Electric Utility Steam Generating Units – Final Report to Congress. US EPA #453/R-98-004. Available at <http://www.epa.gov/ttn/caaa/t3rc.html>.



exposure to chromium compounds. Where the specific compound or oxidation state of chromium is known and available, the appropriate dose response value may be applied for the purposes of risk assessment. However, for generically reported chromium emissions where there is no information provided regarding the oxidation state of the chromium, we generate “default” speciation profiles that reflect the proportions of emissions that would likely be in the Cr(VI) and Cr(III) oxidation states. Appendix A contains a paper by several EPA staff wherein available chromium speciation data for different industrial categories of emission sources have been analyzed to develop default chromium speciation profiles. The following sections describe the data, analyses, limitations and conclusions regarding chromium speciation for the two selected source types of coal-fired and oil-fired boilers.

## 2.4 Chromium Speciation for Specific Source Types

### 2.4.1 Coal Boilers

Based on source test data from 7 units, including 4 utility boilers and 3 industrial boilers (which are similar in process to utility boilers but often smaller), an average of 12 percent hexavalent chromium was derived to be used as the speciation default for coal-fired boilers without available chromium speciation information. The average hexavalent chromium for the 4 utility boilers was 11 percent and the range for the 4 tests was from 0.4 percent to 23 percent.<sup>15</sup> Although the range of values was not reported, the average hexavalent chromium for the 3 industrial boilers was 12 percent. (Emissions database compiled November 30, 2000, in support of National Emission Standards for Hazardous Air Pollutants for Industrial/Commercial/Institutional Boilers and process Heaters, Final Rule, 69FR55217 September 13, 2004). Because of the limited number of units tested, we chose the value of 12 percent (the highest percent average of hexavalent chromium when considering both utility and industrial boilers) to be used as the default for our analysis of potential chromium risks from coal-fired utility boilers.

### 2.4.2 Oil Boilers

Based on source test data from 7 units, an average of 18 percent hexavalent chromium was derived to be used as the speciation default for oil-fired boilers without available chromium speciation information. The average hexavalent chromium for the 7 utility boilers was 18 percent, and the range for the 7 tests was 5 to 34 percent.<sup>16</sup>

---

<sup>15</sup> US EPA, 1998. Study of Hazardous Air Pollutant Emissions from Electric Utility Steam Generating Units – Final Report to Congress. U.S. EPA #453/R-98-004. Available at <http://www.epa.gov/ttn/caaa/t3rc.html>.

<sup>16</sup> US EPA, 1998. Study of Hazardous Air Pollutant Emissions from Electric Utility Steam Generating Units – Final Report to Congress. U.S. EPA #453/R-98-004. Available at <http://www.epa.gov/ttn/caaa/t3rc.html>.

## 2.5 Uncertainties and Limitations

The uncertainties and limitations associated with this analysis are related primarily to the speciation profile data availability, and the assumptions made to generate the default speciation profiles.

Assumptions were made in this analysis in the: 1) selection of the compound species of chromium driving cancer risks based on health effects information, and 2) selection of the appropriate percentage of the chromium species driving cancer risk for derivation of the inhalation cancer risk estimates for chromium emitting facilities. This section briefly describes the assumptions made and associated uncertainties and limitations, and a qualitative characterization of the relative confidence (assigned as low, moderate or high) regarding the used assumptions.

A major limitation of this analysis is the small number of test data (i.e., speciation profile only from 14 units) available to derive chromium default speciation profile values for both coal- and oil- fired EGUs. This data represents a very small portion of the units that exist within the respective source types (approximately 1,200 combined coal- and oil-fired EGUs), which introduces great uncertainties when making generalizations on how accurately the default profiles derived in this analysis reflect actual speciation profiles for coal- and oil-fired EGU emissions. With regard to selecting the appropriate percent of chromium to use in the derivation of default speciation profiles based on the available speciation data, we chose to calculate the percent average based on pooling similar test data from the available units for coal- and oil-fired EGUs. Although this seems to be a reasonable quantitative approach given the limited data set, an alternative, and more conservative, approach would consist on selecting the maximum measured percentage of hexavalent chromium from the available data rather than the average of the range (i.e., selecting 23 percent rather than 12 percent for coal-fired EGUs). Further, speciation information showing coal combustion emissions containing as much as 43 percent hexavalent chromium<sup>17</sup> indicates that past quantitative approaches could, in fact, underestimate hexavalent chromium inhalation risks. However, another study of speciation of chromium in coal combustion showed hexavalent chromium percentage levels close to detection limits (i.e., 3-5 percent of total).<sup>18</sup> Given the high variability across the speciation data available, there is great uncertainty associated with percent hexavalent chromium for either coal- or oil-fired EGUs. Based on the available information, we have low confidence in selecting a single percentage of hexavalent chromium to represent the true composition of chromium in all EGU emissions.

---

<sup>17</sup> Galbreath KC, Zygarlicke CJ. 2004. Formation and chemical speciation of arsenic-, chromium-, and nickel-bearing coal combustion PM<sub>2.5</sub>, *Fuel Process Technol* 85:701-726.

<sup>18</sup> Huggins FE, Najih M, Huffman GP. 1999. Direct speciation of chromium in coal combustion by-products by X-ray absorption fine structure spectroscopy, *Fuel Process Technol* 78:233-242.

With regard to the cancer risk, we selected hexavalent chromium as the species likely to be driving cancer risks based on solid evidence from the health effects database for chromium and compounds. Major scientific bodies that conduct thorough reviews on carcinogenic compounds (e.g., IARC, NTP) agree that there is sufficient evidence for the carcinogenicity of Cr(VI) compounds in humans based on the combined evidence from the epidemiological, animal and mechanistic data available. These reports also state that compounds of chromium III are not classifiable as to their carcinogenicity. Based on this information, we have high confidence on the assumption that hexavalent chromium is the carcinogenic species and that the carcinogenic risk of chromium-emitting facilities is proportional to the mass of hexavalent chromium contained in the emissions from those facilities.

### 2.6 Conclusions

Based on the information above we have high confidence in the assumption that hexavalent chromium is the carcinogenic species driving the risk of chromium-emitting facilities and thus we consider a reasonable approach to derive default speciation profiles based on the mass of hexavalent chromium contained in the emissions from chromium-emitting facilities. Nevertheless, the confidence in the default speciation profiles is low because the profiles are based on a limited data set with a wide range of percentages of hexavalent chromium across the different samples. An alternative, more conservative approach would be to use the maximum measured percentage of hexavalent chromium rather than the highest average of the range observed across samples (i.e., use of 23 percent rather than 12 percent hexavalent chromium).

## 3 Nickel and Compounds

### 3.1 Background

Nickel (Ni) is a lustrous white, hard, ferromagnetic metal found in transition group VIII of the Periodic Table. It has high ductility, good thermal conductivity, high strength, and fair electrical conductivity. It constitutes approximately 0.009 percent of the earth's crust, making it the 24th most abundant element. Nickel can achieve several oxidation states including -1, 0, +1, +2, +3, and +4, and can be combined with many other elements to form different nickel compounds; however, the majority of nickel compounds are nickel +2 species. Indirect sources, primarily coal and oil combustion, are estimated to release from 85 to 94 percent of the total anthropogenic nickel emissions to the air. Nickel compounds are used for nickel alloys, electroplating, batteries, coins, industrial plumbing, spark plugs, machinery parts, stainless-steel, nickel-chrome resistance wires, and as catalysts.<sup>19</sup>

Nickel and nickel compounds have been classified as human carcinogens. National and international scientific bodies including the IARC (1990),<sup>20</sup> the World Health Organization (WHO, 1991),<sup>21</sup> and the European Union's Scientific Committee on Health and Environmental Risks (SCHER, 2006),<sup>22</sup> agree that nickel compounds (including nickel sulfate), in general, are carcinogenic. In their *12<sup>th</sup> Report of the Carcinogens*, the NTP has classified nickel compounds as known to be human carcinogens based on sufficient evidence of carcinogenicity from studies in humans showing associations between exposure to nickel compounds and cancer, and supporting animal and mechanistic data. More specifically, this classification is based on consistent findings of increased risk of cancer in exposed workers, and supporting evidence from experimental animals that shows that exposure to an assortment of nickel compounds by multiple routes causes malignant tumors at various organ sites and in multiple species. The *12<sup>th</sup> Report of the Carcinogens* states that the "combined results of epidemiological studies, mechanistic studies, and carcinogenesis studies in rodents support the concept that nickel compounds generate nickel ions in target cells at sites critical for carcinogenesis, thus allowing consideration and

---

<sup>19</sup> US EPA, 1986. Health Assessment Document for Nickel. EPA/600/8-83/012F. National Center for Environmental Assessment, Office of Research and Development, Washington, DC.

<sup>20</sup> International Agency for Research on Cancer (IARC), 1990. IARC monographs on the evaluation of carcinogenic risks to humans. *Chromium, nickel and welding*. Vol. 49. Lyons, France: International Agency for Research on Cancer, World Health Organization Vol. 49:256.

<sup>21</sup> International Labour Organization/United Nations Environment Programme, World Health Organization (WHO), 1991. Nickel. In Environmental Health Criteria No 108 Geneva.

<sup>22</sup> European Commission, Scientific Committee on Health and Environmental Risks (SCHER), 2006. Opinion on: Reports on Nickel, Human Health part. SCHER, 11th plenary meeting of 04 May 2006 [[http://ec.europa.eu/health/ph\\_risk/committees/04\\_scher/docs/scher\\_o\\_034.pdf](http://ec.europa.eu/health/ph_risk/committees/04_scher/docs/scher_o_034.pdf)].CHER 2006

evaluation of these compounds as a single group”. Although the precise nickel compound (or compounds) responsible for the carcinogenic effects in humans is not always clear, studies indicate that nickel sulfate and the combinations of nickel sulfides and oxides encountered in the nickel refining industries cause cancer in humans. In agreement with the above mentioned scientific bodies, the US Department of Health and Human Services (DHHS, 1994)<sup>23</sup> has determined that nickel compounds are known human carcinogens, and that another nickel compound, nickel metal, may reasonably be anticipated to be a carcinogen. The EPA has only evaluated two nickel compounds for their carcinogenic potential -- nickel subsulfide and nickel refinery dusts -- and has classified them both as group A, human carcinogens. Another assessment for the carcinogenic potential of nickel and nickel compounds has been developed by the California Department of Health Services (CDHS, 1991)<sup>24</sup>. With regard to speciation, it is noted in this assessment that the available epidemiological data is inadequate to develop separate unit risk factors for different nickel compounds, nevertheless the view of CDHS is consistent with consideration of both insoluble and soluble nickel compounds, as a group, as carcinogenic based on the available epidemiological evidence.

The major scientific bodies mentioned above have recognized that there are potential differences in toxicity and/or carcinogenic potential across the different nickel compounds. These differences are believed to be due, in part, to differences in solubility properties and/or different speciation of nickel compounds that in turn make nickel ions be more or less available at target sites. The views of the IARC’s nickel review group (IARC’s Working group Special Report 2009)<sup>25</sup> is that in addition to the release of nickel ions at target sites, there may be other less understood factors that promote accumulation of nickel ions at critical target sites and that given the available scientific evidence, it is difficult to predict the relative carcinogenic hazard of nickel compounds. There have been different views on whether or not nickel compounds, as a group, should be considered as carcinogenic to humans. Some authors believe that water soluble nickel, such as nickel sulfate, should not be considered a human carcinogen, based primarily on a negative nickel sulfate 2-year NTP rodent bioassay (which is different than the positive 2-year NTP bioassay for nickel subsulfide).<sup>26,27,28</sup> Although these authors agree that the epidemiological

---

<sup>23</sup> US Department of Health and Human Services (DHHS), 1994. Seventh annual report on carcinogens: Summary 1994. Research Triangle Park, NC: National Institute of Environmental Health Sciences (NIEHS), 262-269.

<sup>24</sup> California Department of Health Services (CDHS), 1991. Health Risk Assessment for Nickel. Initial Statement for Rulemaking, Proposed Identification of Nickel as a Toxic Air Contaminant – Technical Support Document, part B. Available online at [http://www.arb.ca.gov/toxics/id/summary/nickel\\_tech\\_b.pdf](http://www.arb.ca.gov/toxics/id/summary/nickel_tech_b.pdf).

<sup>25</sup> International Agency for Research on Cancer (IARC) Working Group: Special Report. Policy; A review of human carcinogens; Part C: metals, arsenic, dusts, and fibres. *Lancet Oncol*, 2009, 10:453-454.

<sup>26</sup> Oller A. Respiratory carcinogenicity assessment of soluble nickel compounds. *Environ Health Perspect*, 2002, 110:841-844.

<sup>27</sup> Heller JG, Thornhill PG, Conard BR: New views on the hypothesis of respiratory cancer risk from soluble nickel exposure; and reconsideration of this risk's historical sources in nickel refineries. *J Occup Med Toxicol*, 2009, 4:23.

data clearly supports an association between nickel and increased cancer risks, they sustain that the data are weakest regarding water soluble nickel. A recent review by Grimsrud et al., (2010)<sup>29</sup> highlights the robustness and consistency of the epidemiological evidence across several decades showing associations between exposure to nickel and nickel compounds (including nickel sulfate) and cancer.

As mentioned above, the EPA has only derived URE values for nickel subsulfide and for nickel refinery dusts. Nickel subsulfide has a URE value of 0.00048 per  $\mu\text{g}/\text{m}^3$ , which means that inhaling nickel subsulfide in air at an average concentration of 1  $\mu\text{g}/\text{m}^3$  daily for a lifetime poses an estimated increased risk of cancer of 480 in a million. The nickel refinery dust has a URE value of 0.00024  $\mu\text{g}/\text{m}^3$ , which suggests that this mixture may have half the carcinogenic potency of nickel subsulfide. There are two other available UREs that have both been derived for nickel compounds as a group. One was developed by the California Department of Health Services (CDHS, 1991) and the other by the Texas Commission on Environmental Quality (TCEQ, Development Support Document, 2011)<sup>30</sup>, with values of 0.00026 per  $\mu\text{g}/\text{m}^3$  and 0.00017  $\mu\text{g}/\text{m}^3$ , respectively.

### 3.2 Approach for Estimating Inhalation Cancer Risks from Nickel Compounds

Based on past scientific and technical considerations, the determination of the percent of nickel subsulfide (which has an IRIS URE value) versus nickel sulfate (with no available URE value) was considered a major factor for estimating the extent and magnitude of the risks of cancer due to nickel-containing emissions. Thus, in previous analyses, we estimated cancer risks due to the inhalation of all nickel compounds based on the estimated exposure concentration of nickel subsulfide alone. Thus:

$$\text{Risk} = \text{EC}_{\text{Ni}} * \text{MF}_{\text{Ni subsulfide}} * \text{URE}_{\text{Ni subsulfide}}$$

Where

$\text{EC}_{\text{Ni}}$  is the chronic exposure concentration for the mixture of all nickel compounds,  $\text{MF}_{\text{Ni subsulfide}}$  is the mass percentage of the inhaled mixture which is nickel subsulfide and  $\text{URE}_{\text{Ni subsulfide}}$  which is the cancer unit risk estimate for nickel subsulfide.

---

<sup>28</sup> Goodman JE, Prueitt RL, Thakali S, and Oller AR. The nickel iron bioavailability model of the carcinogenic potential of nickel-containing substances in the lung. *Crit Rev Toxicol* 2011, 41:142-174.

<sup>29</sup> Grimsrud TK and Andersen A. Evidence of carcinogenicity in humans of water-soluble nickel salts. *J Occup Med Toxicol* 2010, 5:1-7. Available online at <http://www.ossup-med.com/content/5/1/7>.

<sup>30</sup> Texas Commission on Environmental Quality (TCEQ), 2011. Development Support Document for nickel and inorganic nickel compounds. Available online at [http://www.tceq.state.tx.us/assets/public/implementation/tox/dsd/final/june11/nickel\\_&\\_compounds.pdf](http://www.tceq.state.tx.us/assets/public/implementation/tox/dsd/final/june11/nickel_&_compounds.pdf)

### 3.3 Approach for Developing Speciation Profiles for Selected Source Types

Similar to chromium, the speciation data for nickel emissions from different source types is limited. Several approaches have been considered by the EPA, over time, in the determination of the cancer risks posed by the inhalation of nickel and nickel compounds emitted by large combustion sources (including oil-combustion). The following subsections describe the data, analyses and assumptions regarding nickel speciation for risk analysis derived in the past (A and B), and (C) potential approaches based on recent nickel speciation data from oil-fired power plants.

#### 3.3.1 A. Approach to Derive Unit Risk Estimates: Electric Utility Report to Congress 1998

A speciation analysis performed by the Electric Power Research Institute<sup>31</sup> using data dated from 1992 to 1994 on 5 sites with oil-fired utilities showed the presence of numerous nickel compounds and a wide range of the percentages of different nickel species measured. This report indicated the following general speciation profile: soluble nickel compounds 25 to 60 percent, sulfidic nickel compounds 4 to 26 percent, metallic nickel compounds 0 to 4 percent, and oxidic nickel compounds 27 to 70 percent. Based on these data, there were two proposed approaches to calculating nickel inhalation risk estimates from these sources. The first approach used the assumption that the mixture of nickel compounds emitted by oil-fired utilities was 50 percent as carcinogenic as nickel subsulfide (the nickel compound with the higher cancer potency based on the existing IRIS UREs). The second approach was also based on the application of the IRIS URE for nickel subsulfide, however it provided a suite of risk estimates depending on the percentage of nickel subsulfide (ranging from 100 to 0 percent) believed to be present in the emissions from oil-fired utilities. The assumption used for both approaches was that only the nickel subsulfide fraction contributes to the cancer risk. The cancer risk due to the other nickel compounds was considered as unknown, and thus not contributing to cancer from nickel-containing emissions.

#### 3.3.2 B. Approach to Derive Unit Risk Estimates: NATA 2000

Based on previous analysis of some of the largest nickel-emitting combustion sources indicating that at least 35 percent of total nickel emissions may be soluble compounds<sup>32</sup>, the EPA assumed that as much as 65 percent of emitted nickel could be in the insoluble form and that all insoluble nickel could be crystalline. Because the URE listed in IRIS for nickel subsulfide represents a form which is pure

---

<sup>31</sup> US EPA, 1998. Study of Hazardous Air Pollutant Emissions from Electric Utility Steam Generating Units – Final Report to Congress. US EPA #453/R-98-004. Available at <http://www.epa.gov/ttn/caaa/t3rc.html>.

<sup>32</sup> US EPA, 2001. National-Scale Air Toxics Assessment for 1996 - Appendix-G: Health Effects Information Used in Cancer and Noncancer Risk Characterization for the NATA 1996 National-Scale Assessment, EPA-453/R-01-003. Available online at <http://www.epa.gov/ttn/atw/sab/appendix-g.pdf>.

insoluble crystalline nickel, this assessment assumed that 65 percent of the total mass of emitted nickel might be of this form, and thus might be carcinogenic. Thus, for the purposes of the 2000 NATA assessment, the EPA assumed that 65 percent of emitted nickel was insoluble, that all insoluble nickel was crystalline, and that the IRIS URE for nickel subsulfide could be applied to this portion.

### **3.3.3 C. Approach to Derive Unit Risk Estimates: Alternatives Based on Speciation of Residual Oil Fly Ashes from Power Plants.**

Recently, a nickel speciation analysis was conducted by the Electric Power Research Institute (EPRI)<sup>33</sup> on residual oil fly ashes (ROFA) obtained from stacks of utility boilers from two of the largest oil-fired power plants in the country, which are located in Hawaii (Honolulu and Waiau, respectively). The ROFA samples were analyzed using x-ray absorption fine structure (XAFS) spectroscopy and x-ray diffraction (XRD). Speciation analysis results indicated that 80 to 95 percent of the total Ni present in the ROFA samples was nickel sulfate hexahydrate ( $\text{NiSO}_4 \cdot 6\text{H}_2\text{O}$ ), and that approximately 20 percent of the total Ni was present as a Ni-containing spinel compound, similar in composition to nickel iron oxide ( $\text{NiFe}_2\text{O}_4$ ). Sulfidic Ni compounds (such as nickel subsulfide) were not detected in this analysis. Given that the ROFA samples tested did not contain nickel subsulfide, using an approach to derive unit risks estimates similar to that used in past analysis (e.g., applying the URE for nickel subsulfide to the mass emissions of all nickel compound) would result in a unit risk estimate equal to zero. Based on what we know regarding the health effects of nickel compounds, as a group, making an assumption of no risk associated with exposure to nickel-containing emissions would clearly not be health-protective. For this reason, we considered the following alternative approaches.

- 1- Using the same approach as 2000 NATA (see above section 3.3.2 B), which consists of using the IRIS URE for nickel subsulfide and assuming that nickel subsulfide constitutes 65 percent of the mass emissions of all nickel compounds. While it does not take the new speciation data into account, this approach was developed for NATA and RTR assessments years ago, and has been peer reviewed by the Science Advisory Board (SAB), each time receiving favorable reviews. It would also help to provide continuity and comparability between current and past assessments. This is the approach used in assessments performed in support of the EPA's Toxics Rule proposed in April 2011.
- 2- Considering a more health-protective approach. Based on the consistent views of major scientific bodies (i.e., NTP in their 12<sup>th</sup> ROC, IARC, and other international agencies) that

---

<sup>33</sup> Energy & Environmental Research Center (EERC), University of North Dakota, Final Report: *Nickel Speciation Analyses of Residual Oil Fly Ashes Using X-Ray Techniques*, 2010. Electronic file available at: [http://oaspub.epa.gov/eims/eimscomm.getfile/?p\\_download\\_id=503933..](http://oaspub.epa.gov/eims/eimscomm.getfile/?p_download_id=503933..)



consider nickel compounds to be carcinogenic, as a group, we propose considering all nickel compounds as carcinogenic as nickel subsulfide. This approach would include the application of the IRIS URE without a factor, assuming 100 percent of nickel compounds as carcinogenic as nickel subsulfide.

- 3- Considering alternative UREs. This approach would involve the direct application of URE values developed for nickel compounds as a group by governmental agencies other than the EPA rather than deriving a value based on the IRIS URE for nickel subsulfide. The application of the CDHS URE or TCEQ URE would yield a unit risk estimate approximately two- to three-fold lower than using 100 percent of the IRIS URE for nickel subsulfide.

### 3.4 Uncertainties and limitations

The uncertainties and limitations associated with these analyses are related primarily to the speciation profile data availability, and the assumptions made to generate the default speciation profiles. Assumptions were made in this analysis to: 1) select the compound species of nickel driving cancer risks based on health effects information, and 2) select the appropriate percentage of the nickel species driving cancer risk for derivation of the inhalation cancer risk estimates for nickel-emitting facilities. This section briefly describes the assumptions made and associated uncertainties and limitations, and a qualitative characterization of the relative confidence (assigned as low, moderate or high) on those assumptions.

Similar to chromium, a major limitation of these analyses is the small number of test data (i.e., three individual nickel speciation analysis of only a few units) available to derive nickel default speciation profile values for coal- and oil-fired units. Another source of great uncertainty is the lack of a speciation profile patterns across the different nickel speciation analysis available, and the wide range of percentages for the individual nickel species. Based on this information, we have low confidence in the derivation of default nickel speciation profiles based on the available speciation data.

With regard to the estimation of cancer risk from inhalation of nickel and compounds, we have in the past selected nickel subsulfide as the species likely to be driving cancer risks based on health effects evidence indicating that nickel subsulfide is carcinogenic in both humans and animals, and on the potentially higher cancer potency of nickel subsulfide when compared to that of nickel refinery dusts (the only other IRIS URE value available for nickel compounds). Although this approach was considered reasonable at the time (and consistent with approaches used for derivation of speciation defaults for other compounds, such as chromium), an alternative and more conservative approach would be based on consideration of all nickel compounds, as a group, to be as carcinogenic as nickel subsulfide.

It is important to note that the three existing URE values (i.e., derived by: IRIS, DCHS or TCEQ with values of 0.00048, 0.00026 and 0.00017  $\mu\text{g}/\text{m}^3$ , respectively), only vary by less than 3-fold, and that using any of these three UREs would yield roughly similar risk estimates.

### 3.5 Conclusion

Based on the views of the most authoritative scientific bodies, the EPA considers all nickel compounds to be carcinogenic, as a group, and does not focus on nickel speciation or solubility as a strong determinant of carcinogenicity. EPA will continue using the current IRIS URE for nickel subsulfide as the preferred value for nickel compounds because IRIS derived values are at the top of our hierarchy with respect to dose response information used in EPA's risk characterizations. Nevertheless, taking into account that there may be differences in toxicity and/or carcinogenic potential across mixtures of different nickel compounds, and given that there have been two URE values derived for exposure to mixtures of nickel compounds that are 2-3 fold lower than the IRIS URE for nickel subsulfide, the EPA also considers it reasonable to use a value that is 50 percent of the IRIS URE for nickel subsulfide for providing an estimate of the lower end of a plausible range of cancer potency values for different mixtures of nickel compounds.

---

United States  
Environmental Protection  
Agency

Office of Air Quality Planning and Standards  
Health and Environmental Impacts Division  
Research Triangle Park, NC

Publication No. EPA-452/R-11-012  
[October, 2011]

---