Before we can harvest knowledge in the field of healthcare, we first need to ensure that the right seeds are sown.

Areas of activity

Optimum healthcare
What is the optimum result of cure and care in view of the risks and opportunities?

Prevention
Which forms of prevention can help realise significant health benefits?

Healthy nutrition
Which foods promote good health and which carry certain health risks?

Environmental health
Which environmental influences could have a positive or negative effect on health?

Healthy working conditions
How can employees be protected against working conditions that could harm their health?

Innovation and the knowledge infrastructure
Before we can harvest knowledge in the field of healthcare, we first need to ensure that the right seeds are sown.

Advisory Reports

The Health Council’s task is to advise ministers and parliament on issues in the field of public health. Most of the advisory opinions that the Council produces every year are prepared at the request of one of the ministers.

In addition, the Health Council issues unsolicited advice that has an ‘alerting’ function. In some cases, such an alerting report leads to a minister requesting further advice on the subject.

Health-based recommendation on occupational exposure limits

Hexavalent chromium compounds

2016/13E

Hexavalent chromium compounds

Health Council of the Netherlands

www.healthcouncil.nl
Health Council of the Netherlands

Hexavalent chromium compounds

Health-based recommendation on occupational exposure limits
Dear Minister,

I hereby submit the advisory report on the effects of occupational exposure to hexavalent chromium compounds.

This advisory report is part of an extensive series in which carcinogenic substances are evaluated for the possibility to establish health-based occupational cancer risk values in accordance with European Union guidelines. This involves substances to which people can be exposed under working conditions.

The advisory report was prepared by the Dutch Expert Committee on Occupational Safety (DECOS) of the Health Council. The advisory report has been assessed by the Health Council’s Standing Committee on Public Health.

In this report, the Committee concludes that hexavalent chromium compounds are carcinogenic substance and that the underlying processes include a stochastic genotoxic mechanism. The Committee estimated that the additional lifetime cancer risk for hexavalent chromium compounds amounts to:

- $4 \times 10^{-5}$ for 40 years of occupational exposure to $0.01 \mu g/m^3$
- $4 \times 10^{-3}$ for 40 years of occupational exposure to $1 \mu g/m^3$.

I have today sent copies of this advisory report to the State Secretary of Infrastructure and the Environment and to the Minister of Health, Welfare and Sport, for their consideration.

Yours sincerely,

Professor J.L. Severens
Vice President
Hexavalent chromium compounds

Health-based recommendation on occupational exposure limits

Dutch Expert Committee on Occupational Safety (DECOS),
a Committee of the Health Council of the Netherlands

to:

the Minister of Social Affairs and Employment

The Health Council of the Netherlands, established in 1902, is an independent scientific advisory body. Its remit is “to advise the government and Parliament on the current level of knowledge with respect to public health issues and health (services) research...” (Section 22, Health Act).

The Health Council receives most requests for advice from the Ministers of Health, Welfare and Sport, Infrastructure and the Environment, Social Affairs and Employment, and Economic Affairs. The Council can publish advisory reports on its own initiative. It usually does this in order to ask attention for developments or trends that are thought to be relevant to government policy.

Most Health Council reports are prepared by multidisciplinary committees of Dutch or, sometimes, foreign experts, appointed in a personal capacity. The reports are available to the public.

This report can be downloaded from www.healthcouncil.nl.

Preferred citation:

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Executive summary

At the request of the Minister of Social Affairs and Employment, the Dutch Expert Committee on Occupational Safety (DECOS), a Committee of the Health Council of the Netherlands, derives so-called health-based calculated occupational cancer risk values (HBC-OCRVs), which are exposure levels that correspond to excess cancer risk levels of 4 per 1,000 and 4 per 100,000 due to occupational exposure. It involves substances which are classified by the Health Council or the European Union in category 1A or 1B, and which are considered stochastic genotoxic carcinogens. For the risk estimation, the Committee uses the Guideline for the calculation of occupational cancer risk values of the Health Council. In this report the Committee evaluates the possibility to establish such estimates for hexavalent chromium compounds. Hexavalent chromium compounds are used as anti-corrosives, in the manufacturing and welding of stainless steel, as color pigments, in chrome plating, tanning and wood preservation.

In this report, DECOS concludes that all hexavalent chromium compounds are carcinogenic substances and that the underlying processes include a stochastic genotoxic mechanism. Based on epidemiological data the Committee estimates that the additional lifetime cancer risk for hexavalent chromium compounds amounts to:

- $4 \times 10^{-5}$ for 40 years of occupational exposure to $0.01 \mu g/m^3$
- $4 \times 10^{-3}$ for 40 years of occupational exposure to $1 \mu g/m^3$. 
These values are similar to the risks calculated by the European Chemicals Agency (ECHA) and the German Ausschuss für Gefahrstoffe (AGS).²³
Chapter 1

Scope

1.1 Background

At the request of the Minister of Social Affairs and Employment (Annex A), the Dutch Expert Committee on Occupational Safety (DECOS) (Annex B), a Committee of the Health Council of the Netherlands, performs scientific evaluations of the toxicity and carcinogenicity of substances to which man can be exposed at the workplace. The purpose of these evaluations is to recommend a health-based recommended occupational exposure limit (HBROEL) or health-based calculated occupational cancer risk values (HBC-OCRV) for the concentration of the substance in air, provided the database allows the derivation of such values. These recommendations serve as a basis in setting legally binding limit values by the minister. As a preference, the minister has requested the Health Council to align, if possible, with the evaluations of other European organizations.

In the present advice, the Committee re-assesses the risk of (lung) cancer after occupational exposure to hexavalent chromium compounds. For exposure at the workplace the most important hexavalent chromium compounds are chromium trioxide (CrO$_3$), and the mono- ($\text{CrO}_4^{2-}$) and dichromates (Cr$_2$O$_7^{2-}$). Cromium VI-compounds are used as anti-corrosives, in the manufacturing and welding of stainless steel, color pigments, in chrome plating, tanning and wood preservation. Individual hexavalent chromium compounds differ in water
solubility varying between very poorly soluble to highly soluble (see Annex D, Table 2).

DECOS published for the first time a report on hexavalent chromium in 1985. This report was reevaluated in 1998. In 2004 the health risks of occupational exposure to hexavalent chromium compounds were evaluated by the Scientific Committee on Occupational Exposure Limits (SCOEL). Recently, the Committee for Risk Assessment (RAC) with the European Chemicals Agency (ECHA) (in 2013) and the German Ausschuss für Gefahrstoffe (AGS) from the Bundesanstalt für Arbeitsschutz und Arbeitsmedizin (BAuA) (in 2014), have quantified the health risks of occupational exposure to hexavalent chromium compounds. Of recent date are also the quantitative evaluations of cancer risk published by the US NIOSH (2013) and the group of Seidler et al. (2013).

1.2 Committee, methods and data

DECOS has re-evaluated its previous advice on hexavalent chromium compounds (1998) taking into account the published literature on toxicity and carcinogenicity until August 2016 and the abovementioned evaluations. This advice describes the results of the evaluation of DECOS. The members of DECOS are listed in Annex B. In January 2015, DECOS released a draft version of the report for public review. The individuals and organisations that commented on the draft are listed in Annex C. DECOS has taken these comments into account in finalising its report. In Annex G the critical data used by DECOS for its quantitative risk assessment are summarized.
Carcinogenic classification and mechanism of genotoxicity

The basis for the carcinogenic classification of hexavalent chromium compounds has been established by the International Agency for research on Cancer (IARC) in 1990. IARC concluded then that there was ‘sufficient evidence’ to consider hexavalent chromium to be carcinogenic in both humans and experimental animals and that classification in category 1 was justified (‘carcinogenic to humans’). This IARC classification was again confirmed in 2009 (Straif et al.) and 2012 (IARC 100C).

Most hexavalent chromium compounds are classified by the European Union for carcinogenicity in category 1B (‘substance presumed to be carcinogenic to humans’). Exceptions are chromium trioxide, zinc chromate and zinc potassium chromate classified in category 1A (‘substance known to be carcinogenic to humans’).

First DECOS investigated whether it could agree with the carcinogenic classification of hexavalent chromium compounds by the European Union. DECOS therefore discussed all relevant animal and human studies (until November 2015) in its meetings. DECOS observes that after publication of the previous advice (1998) only a limited number of experimental animal studies but a significant number of human studies have been published (and summarized by IARC (2012), NIOSH (2013), NTP 2014).
After evaluation of these studies DECOS concludes that the evidence that hexavalent chromium compounds are carcinogenic in experimental animals and in humans is convincing and agrees with the EU classifications (see also Annex E).

In addition DECOS evaluated the in vitro and in vivo studies on the mechanism of genotoxicity.\textsuperscript{10,29,30} DECOS notes that hexavalent chromium compounds are able to damage DNA in different ways and concludes that the underlying mechanisms are mainly non-stochastic in nature, but can also be stochastic. In case of stochastic genotoxic mechanisms, cancer may develop at any level of exposure, while in case of non-stochastic genotoxic mechanisms safe exposure thresholds could exist. DECOS applies the precaution principle according to its guideline and follows a ‘worst case scenario’ for the risk calculation, taking the stochastic genotoxic mechanism as starting point.\textsuperscript{1} This implies the application of linear extrapolation and the assessment of health-based calculated cancer risk values; the exposure concentrations in air that relate to an additional cancer risk of 4 per 1,000 and 4 per 100,000 due to occupational exposure. These cancer risk values are considered the scientific basis for legally binding exposure limits established by the Minister.
Previous advice of the Health Council and current exposure limit in the Netherlands

3.1 DECOS (1998)

In its previous advice (1998) DECOS based its evaluation of hexavalent chromium compounds on reviews from IARC (1990), WHO (1988), EPA (1984), Wibowo (1993), Langård (1993) and on additional literature from 1986 until 1998. DECOS reported that exposure to hexavalent chromium compounds may lead to lung cancer, nephrotoxicity, hypersensitivity, corrosion of the skin, and irritation of the respiratory and gastrointestinal tracts. DECOS then selected carcinogenicity of the lung as the critical effect for its risk assessment.

DECOS considered all hexavalent chromium compounds as carcinogenic, and was of the opinion that for risk assessment a ‘worst case’ approach was necessary.

Eventually DECOS decided to use the data from the epidemiological study by Mancuso (1975), as adjusted by EPA (1984), as basis for human risk assessment. Mancuso studied 332 white males employed in a chromate producing industry in the US (Painesville, Ohio) between 1931 and 1937 and followed until 1975. Using a linear extrapolation model it was calculated that exposure to 8 \( \mu g/m^3 \) would lead to an additional risk of cancer mortality of \( 1.4 \times 10^{-2} \). DECOS then estimated that the additional lifetime cancer mortality risk for hexavalent chromium compounds amounted to:
- $4 \times 10^{-5}$ for 40 years of occupational exposure to $0.02 \, \mu g/m^3$
- and $4 \times 10^{-3}$ for 40 years of occupational exposure to $2 \, \mu g/m^3$.

[See the DECOS report (1998) and the EPA report (1984) for the conditions of the extrapolation model and details of the calculation.]

3.2 Current exposure limits in the Netherlands

In 2007 the formal exposure limits for soluble hexavalent chromium compounds including chromium trioxide were established at $25 \, \mu g/m^3$ inhalable fraction as time weighted average over 8 hr (TWA-8 hr) and at $50 \, \mu g/m^3$ inhalable fraction as TWA-15 min. (See https://www.ser.nl/, consulted on September 8, 2016).

In addition, in 2007, for the poorly soluble calcium-, strontium- and zinc chromate a TWA-15 min of $10 \, \mu g/m^3$ is reported, while for the very poorly soluble barium- and lead chromate a TWA-15 min of $25 \, \mu g/m^3$ is reported. These latter values originate from the earlier DECOS report in 1985.

In 2013 the Social Economic Council of the Netherlands (SER) advised the minister, after considering the abovementioned advice of SCOEL (2004), to lower the exposure limits for soluble hexavalent chromium compounds and to establish them at $10 \, \mu g/m^3$ (TWA-8 hr) and at $20 \, \mu g/m^3$ (TWA-15 min), and to introduce a TWA-8hr of $50 \, \mu g/m^3$ for poorly soluble hexavalent chromium compounds (see https://www.ser.nl, consulted on September 10, 2016). This advice by the SER has been implemented in 2015.

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16 Hexavalent chromium compounds
4 Evaluations of other international organizations

4.1 SCOEL (2004)

In 2004, the Scientific Committee on Occupational Exposure Limits (SCOEL) published an evaluation of the then existing toxicological literature on hexavalent chromium compounds. The SCOEL made use of a number of reviews (IARC, 1990; Cross et al., 1997; ATSDR, 2000; EPA, 1998) and additional literature up to 2004. The SCOEL reported, as DECOS did in 1998, that exposure to hexavalent chromium compounds may lead to lung cancer, nephrotoxicity, hypersensitivity, corrosion of the skin, irritation of the respiratory and gastrointestinal tracts. The SCOEL decided that carcinogenicity was the critical effect of hexavalent chromium compounds. The SCOEL (2004) then agreed with the classification of hexavalent chromium compounds by the EU.

The SCOEL eventually based its quantitative risk assessment on the combined epidemiological data from ten cohort studies concerning employees occupationally exposed to chromate. These epidemiological studies were previously selected (mainly because of their size) by Steenland et al. in 1996 for a meta-analysis (Enterline, 1974; Hayes et al., 1979; Alderson et al., 1981; Satoh et al., 1981; Korallus et al., 1982; Frentzel-Beyme, 1983; Davies, 1984a and b; Sorahan et al., 1987; Hayes et al., 1989; Takahashi et al., 1990). In addition to the analysis by Steenland et al. the SCOEL calculated cancer risk values for three different scenario’s of exposure (500, 1,000 and 2,000 µg/m³ for 15 years; cumulative 7,500, 15,000 and 30,000 µg x m⁻³ x year). In its final
recommendation the SCOEL decided to follow the first scenario and estimated that approximately 5-28 extra cases of cancer mortality would occur in a cohort of 1,000 employees, followed from age 20 to 85 and exposed to retirement at age 65.

- At an exposure level of 25 µg/m$^3$ this was estimated to be 2-14 extra mortality cases
- at an exposure level of 10 µg/m$^3$ this estimate was 1-6 extra mortality cases
- at 5 µg/m$^3$ this estimate was 0.5-3 extra mortality cases
- and at 1 µg/m$^3$ this estimate was 0.1-0.6.

The SCOEL observed that poorly soluble hexavalent chromium compounds may be less carcinogenic than soluble hexavalent chromium compounds, although this is not quantifiable. The SCOEL proposed therefore to distinguish between exposure limits for poorly soluble hexavalent chromium compounds (TWA-8 hr of 50 µg/m$^3$) and readily soluble hexavalent chromium compounds (TWA-8 hr of 10 µg/m$^3$ and TWA-15 min of 25 µg/m$^3$). [See the SCOEL advice and the study by Steenland et al. for details of the calculation.] The recommendations made by the SCOEL were taken into account in the abovementioned SER advice.

4.2 RAC-ECHA (2013)

The Committee for Risk Assessment (RAC) recently agreed on a proposal prepared by the ECHA secretariat to set dose-response relationships for the (lung and intestinal) carcinogenicity of hexavalent chromium substances.

A review was performed of the carcinogenic dose-responses of 14 hexavalent chromium compounds. Dose-response relationships were derived by linear extrapolation. Extrapolating outside the range of observation inevitably introduces uncertainties. As the mechanistic evidence is suggestive of non-linearity, it is acknowledged that the excess risks in the low exposure range might be an overestimate.

Based on human epidemiology data for the respirable particulate fraction and linear extrapolation, using the analyses by Seidler et al. (2012) on the literature from the Baltimore cohort (Park et al., 2004) and the Painesville cohort (Crump et al., 2003; Luippold et al., 2003) (see paragraph 5.1), and against a background, cumulative lifetime lung cancer risk of 48 per 1,000 for the EU male population, and an 89-year life expectancy, risk estimates were established for workers.

This excess risk linear function was derived from a relative risk (RR) of about 2 at the cumulative exposure of 0.5 mg Cr VI/m$^3$/year, equivalent to a RR
risk of 2 for exposure to 12.5 µg Cr VI/m³ for 40 years. The associated excess lifetime risk (ELR) at this cumulative exposure for a RR of 2 was determined by multiplying the excess RR (RR-1) by the background lung cancer risk in the EU population (Po) according to the equation: ELR(x) = Po(RR-1), where Po = 0.05. This resulted in a excess lifetime risk of 50 x10⁻³ at 12.5 µg Cr VI/m³ for 40 years which is
• equivalent to an excess lifetime risk of 4 x 10⁻³ at 1 µg Cr VI/m³ for 40 years
• and an excess lifetime risk of 4 x 10⁻⁵ at 0.01 µg Cr VI/m³ for 40 years.

4.3 AGS (2014)

In 2014 the Ausschuss für Gefahrstoffe (AGS) published a report based on the evaluation of existing human and experimental toxicological literature.³ The AGS (2014) confirmed the EU classification of hexavalent chromium compounds. According to the AGS both direct genotoxic mechanisms and mechanisms affecting tumour initiation and promotion underlie the carcinogenicity of all hexavalent chromium compounds.

For the quantitative risk assessment the AGS selected the study by Birk et al. (2006), which reported the German part of the multi-plant study by Mundt et al. (2002).¹⁵,²⁵ This study involved 739 employees in the chromate production in Leverkusen en Uerdingen. In this study an increase in lung cancer mortality was observed (22 cases). The exposure in this study was established by measuring the concentrations of chromium in urine and converting these values into corresponding concentrations of hexavalent chromium in air. Eventually, the AGS concluded that occupational exposure to 12.5 µg/m³ would potentially lead to a doubling of the lung cancer risk (5/100). The AGS derived a cancer risk value of
• 4 per 1,000 (4 x 10⁻³) at 40 year occupational exposure to 1 µg/m³.

The AGS did not extrapolate to lower exposure levels because of the uncertainty related to the shape of the dose-effect relationship and the uncertainty in the outcome of the risk calculation. [See the AGS advice and the study by Birk et al. for details of the calculation.³,¹⁵]

4.4 NIOSH (2013)

The US National Institute for Occupational Safety and Health (NIOSH) published a criteria document containing a quantitative risk assessment for
hexavalent chromium compounds in 2013. NIOSH summarized in its report existing human and experimental animal studies. NIOSH used human data for the quantitative risk assessment. Data were considered from two American cohorts of employees in the chromate industry (in Baltimore, Maryland and in Painesville, Ohio respectively). NIOSH used the data of Gibb et al. (2000)(Baltimore cohort) to conduct its risk assessment (Park et al. 2004). This involved a cohort of 2,357 employees in the chromate production industry with 122 mortality cases from lung cancer. NIOSH selected Gibb et al. (2000) because of the quality of the exposure data, the large number of mortality cases, detailed data on smoking and a better retrospective archive of exposure data. NIOSH used a linear extrapolation model and calculated an extra cancer mortality risk of

- 255 per 1,000 exposed to 52 µg Cr VI/m³ during a working life
- 6 per 1,000 at 1 µg/m³
- and approximately 1 per 1,000 at 0.1 µg/m³ (=Recommended Exposure Limit (REL)).

[See the NIOSH criteria document (2013) and the study by Park et al. (2004) for details of the calculation.]
5.1 Risk evaluation

DECOS has drafted a guideline for the calculation of risks of (developing or dying from) cancer as a consequence of occupational exposure. DECOS calculates cancer risk values preferably based on epidemiological data, as this type of data does not involve the uncertainties associated with biological differences between animals and humans. Moreover, the exposure conditions in epidemiological research are generally, in contrast to animal studies, a good representation of the exposure conditions at the workplace. Animal data are therefore considered for risk assessment only if no (reliable) epidemiological data are available.

Only very limited animal data have been published since the publication of the DECOS report in 1998. However, a multitude of new and re-analysed human data and risk assessments have appeared in the literature (IARC (2012), NIOSH (2014), NTP (2014)). In this regard DECOS points at a comparative review of the published quantitative risk estimates for hexavalent chromium in the AGS report (see Table 1). For good comparison, all these estimates are recalculated to express the excess risks per 1,000 individuals occupationally exposed to 1 µg/m³ for 40 years. In addition, the historical data used for each risk assessment are specified in the table. DECOS notes that all the cancer risks, irrespective of the advantages and disadvantages of the database and methods of calculation, are generally in the same order of magnitude (see Table 1).
After evaluation of all abovementioned epidemiological studies, DECOS is of the opinion that data from only a limited number of cohorts are suitable for a reliable risk assessment. [In this regard DECOS shares the opinion of AGS and NIOSH]. These are the American ‘Baltimore cohort’ (Hayes et al., 1979; Braver et al., 1985; Gibb et al., 2000), the American ‘Painesville cohort’ (Mancuso, 1975; Mancuso, 1997; Luippold et al., 2003), and an American (Texas & North Carolina) (Luippold et al., 2005) and a European cohort (Leverkusen & Uerdingen) (Birk et al., 2006) involving employees participating in a ‘multiplant study’ (Mundt et al., 2002). These four cohorts consist of employees in the chromate production industry, show an increased lungcancer risk (except the study by Luippold et al. (2005), exclude smoking as cause of lung cancer and have used a well documented database of exposure measurements.

In a next step, DECOS has investigated whether use could be made of one of the existing risk assessments based on the abovementioned cohorts. Initially,

<table>
<thead>
<tr>
<th>Author</th>
<th>Database</th>
<th>Risk per 1,000 at exposure to 1 µg/m³ during 40 yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>EPA, 1984 &amp; GBBS, 1998</td>
<td>Epidemiology, Painesville (Mancuso, 1975)</td>
<td>2</td>
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<tr>
<td>Sorahan, 1998b</td>
<td>Epidemiology (Sorahan, 1998a,b)</td>
<td>0.8-8</td>
</tr>
<tr>
<td>Crump, 2003</td>
<td>Epidemiology, Painesville (Luippold, 2003)</td>
<td>2</td>
</tr>
<tr>
<td>SCOEL, 2004</td>
<td>Epidemiology (Enterline 1974; Hayes et al., 1979; Alderson et al., 1981; Satoh et al., 1981; Korallus et al., 1982; Frentzel-Beyme, 1983; Davies, 1984a en b, Sorahan et al., 1987; Hayes et al., 1989; Takahashi et al., 1990)</td>
<td>0.1-0.6</td>
</tr>
<tr>
<td>Goldbohm, 2006</td>
<td>Epidemiology (Mancuso, 1997; Gibb, 2000; Crump, 2003)</td>
<td>3-16</td>
</tr>
<tr>
<td>OSHA, 2006</td>
<td>Epidemiology (‘preferred cohorts’: Gibb, 2000; Luippold, 2003)</td>
<td>2-9</td>
</tr>
<tr>
<td>Roller, 2006</td>
<td>Epidemiology (Braver, 1985; Gibb, 2000; Mancuso, 1997; Luippold, 2003; Sorahan, 1998a,b)</td>
<td>2</td>
</tr>
<tr>
<td>Pesch, 2008</td>
<td>Epidemiology (Gibb, 2000; Park, 2006; Luippold, 2003/05; Birk, 2006)</td>
<td>Not quantifiable</td>
</tr>
<tr>
<td>Seidler, 2013 (see also Pesch, 2013 and Seidler, 2013)</td>
<td>Epidemiology, Baltimore (Gibb, 2000; Park, 2004; Park, 2006), Painesville (Crump, 2003; Luippold, 2003)</td>
<td>4</td>
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<tr>
<td>NIOSH-CDC, 2013</td>
<td>Epidemiology, Baltimore (Gibb, 2000, Park, 2004)</td>
<td>6</td>
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<tr>
<td>RAC-ECHA, 2013</td>
<td>Epidemiology (Seidler, 2013)</td>
<td>4</td>
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<tr>
<td>AGS, 2014</td>
<td>Epidemiology, ‘Multiplant’ (Birk, 2006)</td>
<td>4</td>
</tr>
</tbody>
</table>

Table I: Extra lung cancer risk at occupational exposure to chromium VI compounds (based on AGS 2014, modified by DECOS 2016).
DECOS confined itself to the European risk assessments by the SCOEL, RAC-ECHA and the AGS.

The report of the SCOEL is based on a meta-analysis of relatively dated epidemiological studies. For some of these studies a follow-up has been published in the meantime. The studies were selected by SCOEL mainly based on size, but studies were included that did not report solid data on exposure level and duration. In the meta-analysis performed by the SCOEL each individual study included contributed equally, for one single average value, to the analysis, while the SCOEL did not consider the internal exposure-response relationship for each study. These choices in methodology do not align with the current scientific view of DECOS, in which the evaluation of the quality of each individual study serves as starting point.

In the risk assessment by the AGS, which is based on the epidemiological study by Birk et al., the exposure data used were established by biomonitoring chromium in urine, which is in contrast to other studies. Subsequently these urine chromium values were converted into concentrations in air. The assumption made by the AGS that measurement of total chromium (Cr VI+Cr III) in urine mainly reflects the exposure to hexavalent chromium is considered by DECOS to be a significant uncertainty. Also the shape of the exposure-risk relationship in the lower exposure concentrations is not very clear from the AGS study but may be sublinear which leads to uncertainties in the results after linear extrapolation. Apparently, this is the reason that the AGS did not calculate the extra risk at the lower chromium concentrations. Based on these abovementioned considerations regarding the SCOEL and AGS reports DECOS has decided to explore further options.

The methodology as applied in the risk assessment made by Seidler et al. (2013) and subsequently processed by RAC-ECHA, is generally in line with the recent DECOS guideline and scientific views. First Seidler et al. evaluated all existing epidemiological studies regarding exposure to hexavalent chromium at work and the risk of lung cancer. These studies were evaluated based on compliance with previously defined quality criteria, the use of data regarding more than one exposure level and the correction for the effect of smoking on the development of cancer. Based on these inclusion criteria Seidler et al. selected five studies to establish an exposure-effect relationship (Gibb et al. (2000), Park et al. (2004) and Park & Stainer (2006) from the Baltimore cohort); Crump et al. (2003) and Luippold et al. (2003) from the Painesville cohort). In a subsequent meta-analysis an average dose-effect relationship was calculated, applying linear models, for the Crump (2003) and the Park (2004) studies.
Thereafter, Seidler et al. (2013) calculated an extra lung cancer risk for hexavalent chromium compounds of 4 per 10,000 (4 x 10\(^{-4}\)) after 40 year occupational exposure to 0.1 µg/m\(^3\) and 4 per 1,000 (4 x 10\(^{-3}\)) after 40 year occupational exposure to 1 µg/m\(^3\). [See the study by Seidler et al. (2013) for details of the calculation.\(^8\)] DECOS considered it important that the calculations are based on multiple studies when possible (and thus not only by the study of Park (2004) as has been done in the risk assessment by NIOSH (2013)).\(^7,52\) Therefore DECOS prefers the study by Seidler et al. as starting point for its further risk assessment.

As a first step DECOS checked the calculations by Seidler et al. Based on the average slope of the dose-effect relationship of the two selected studies in the meta-analysis an extra risk was calculated for 40 years exposure, during the ages 20-60, and a latency period of 10 years. This resulted in extra risks of 4 per 10,000 and 4 per 1,000 for exposure to hexavalent chromium concentrations of 0.1 µg/m\(^3\) and 1 µg/m\(^3\), respectively, up to age 75 years and using European (male) mortality data for lung cancer.

Subsequently, DECOS performed calculations using mortality data from the Netherlands’ population (from 2000 to 2010), separated by age and sex). Moreover, the cancer risk values were calculated taking into account a higher age (end of cohort at 100 years) (see Annex F). This resulted into extra risks of respectively

- 4 per 100,000 at exposure to 0.0104 µg/m\(^3\)
- and 4 per 1,000 at exposure to 1.04 µg/m\(^3\).

These exposure levels are almost equal to those calculated by Seidler et al. DECOS notes that the expected higher risks at higher age are probably compensated because male and female mortality data are combined in the DECOS calculation. When using only male mortality data, as was done by Seidler et al., the DECOS calculation would lead to an approximately 28% lower exposure level. [See Annex G for details of the calculation.]

In addition, DECOS notes that the calculated exposure of 1 µg/m\(^3\) at an extra risk of 4 per 1,000 (based on the Seidler et al. data) equals the exposure calculated by the RAC-ECHA (also based on the Seidler et al. data) and the AGS (based on the data by Birk et al.).\(^2,3,8,15\)

The abovementioned health-based calculated cancer risk values (HBC-OCRVs) are based on exposure of employees in the chromate producing industry. However, the epidemiological data do not allow to differentiate the cancer risks...
between individual hexavalent chromium compounds, for instance because of solubility or bioavailability. Therefore DECOS investigated whether data from animal and/or in vitro studies could support the differentiation of the abovementioned human risk assessment for individual hexavalent chromium compounds.

DECOS notes that since the publication of its previous advice no new critical animal experiments have been published. Earlier animal studies point out that hexavalent chromium compounds are carcinogenic by inducing tumors in the lung after inhalatory (Glaser et al. 1985, 1986; Nettlesheim et al., 1971; Adachi et al., 1986; Adachi, 1987), intratracheal (Steinhoff et al., 1986) and intrabronchial administration (Steinhoff et al., 1986). Also, upon administration via other routes (for instance orally) hexavalent chromium appears to be carcinogenic. The animal experiments suggest that differences exist in the carcinogenic potential of the various hexavalent chromium compounds, which are probably related to solubility and bioavailability. However, the variation in the experimental designs of the animal studies and the lack of reliable data regarding poorly soluble hexavalent chromium compounds do not allow a clear conclusion on the nature of these interference (IARC (1980, 1990, 2012), SCOEL (2004), DECOS (1998)).

The NIOSH report mentions explicitly that animal experiments do not exclude the possibility that poorly soluble hexavalent chromium compounds are equally carcinogenic as, or even more carcinogenic than, soluble hexavalent chromium compounds.

DECOS, however, chooses the ‘worst case approach’ and prefers not to differentiate between individual hexavalent chromium compounds in the risk assessment. DECOS concludes that data from carcinogenicity studies in experimental animals do not give reason to adjust the abovementioned human risk assessment.

DECOS also notes that hexavalent chromium compounds generally give positive results for mutagenicity and clastogenicity in a multitude of genotoxicity tests. A number of these genotoxicity studies suggests differences in genotoxic potential of hexavalent chromium compounds based on solubility (IARC (1990), SCOEL (2004), DECOS (1998)). However, these differences have never been unequivocally confirmed. Therefore, it is not possible to exclude compounds because of absence of mutagenic or clastogenic potential (DECOS (1998), SCOEL (2014)).

Eventually DECOS concludes that all hexavalent chromium compounds should be considered as carcinogens, and that in the health-based cancer risk calculation no distinction should be made between soluble and poorly soluble hexavalent chromium compounds. DECOS shares this opinion with the AGS.
However, doing so DECOS does not share the opinion of the SCOEL (2004).13-8

5.2 **Groups with increased risk**

No indications were found by DECOS for the existence of special (sub)populations with a possible increased lung cancer risk after exposure to hexavalent chromium compounds.

5.3 **Conclusions and recommendation**

The Minister of Social Affairs and Employment requested the Health Council to establish occupational exposure limits for hexavalent chromium compounds and to align, if possible, with evaluations of other – preferably European organisations – such as the SCOEL and the AGS.

DECOS notes that after publication of the previous advice (1998) a multitude of new and newly analysed human data for quantitative risk assessment have been published. Moreover, DECOS observes that in the last decade a large number of quantitative risk assessments has been published with calculated cancer risks generally in the same order of magnitude (see Table 1). DECOS is of the opinion that the meta-analysis by Seidler et al. (2013) is the best starting point for a quantitative risk assessment.

DECOS concludes that all hexavalent chromium compounds should be considered as carcinogens, that underlying processes include a stochastic genotoxic mechanism, and that in the health-based cancer risk calculation no distinction should be made between soluble and poorly soluble hexavalent chromium compounds.

After performing additional calculations using the data by Seidler et al. DECOS estimates that the additional lifetime cancer risk for hexavalent chromium compounds amounts to:

- 4 x 10⁻⁵ for 40 years of occupational exposure to 0.01 µg/m³
- 4 x 10⁻³ for 40 years of occupational exposure to 1 µg/m³.

These values correspond to the risks calculated by the European Chemicals Agency (ECHA) and the German Ausschuss für Gefahrstoffe (AGS).2,3
Literature


6. SCOEL (Scientific Committee on Occupational Exposure Limits EC. Hexavalent Chromium. 2004: SCOEL/SUM/86.


Hexavalent chromium compounds
31 EPA (Environmental Protection Agency). Health Assessment Document for Chromium. US Environmental Protection Agency; 1984: EPA-600/8-83-014F.
30 Hexavalent chromium compounds


A Request for advice
B The Committee
C Comments on the public review draft
D Water solubility of hexavalent chromium compounds
E Carcinogenic classification of substances by the Committee
F Health-based occupational cancer risk calculations
G Critical data for the health-based calculation of the cancer risk values for hexavalent chromium compounds

Annexes
In a letter dated October 11, 1993, ref DGA/G/TOS/93/07732A, to, the State Secretary of Welfare, Health and Cultural Affairs, the Minister of Social Affairs and Employment wrote:

Some time ago a policy proposal has been formulated, as part of the simplification of the governmental advisory structure, to improve the integration of the development of recommendations for health based occupation standards and the development of comparable standards for the general population. A consequence of this policy proposal is the initiative to transfer the activities of the Dutch Expert Committee on Occupational Standards (DECOS) to the Health Council. DECOS has been established by ministerial decree of 2 June 1976. Its primary task is to recommend health based occupational exposure limits as the first step in the process of establishing Maximal Accepted Concentrations (MAC-values) for substances at the work place.

In an addendum, the Minister detailed his request to the Health Council as follows:

The Health Council should advice the Minister of Social Affairs and Employment on the hygienic aspects of his policy to protect workers against exposure to chemicals. Primarily, the Council should report on health based recommended exposure limits as a basis for (regulatory) exposure limits for air quality at the work place. This implies:

• A scientific evaluation of all relevant data on the health effects of exposure to substances using a criteria-document that will be made available to the Health Council as part of a specific request for advice.
• If possible this evaluation should lead to a health based recommended exposure limit, or, in the case of genotoxic carcinogens, a ‘exposure versus tumour incidence range’ and a calculated concentration in air corresponding with reference tumour incidences of $10^{-4}$ and $10^{-6}$ per year.

• The evaluation of documents review the basis of occupational exposure limits that have been recently established in other countries.

• Recommending classifications for substances as part of the occupational hygiene policy of the government. In any case this regards the list of carcinogenic substances, for which the classification criteria of the Directive of the European Communities of 27 June 1967 (67/548/EEG) are used.

• Reporting on other subjects that will be specified at a later date.

In his letter of 14 December 1993, ref U 6102/WP/MK/459, to the Minister of Social Affairs and Employment the President of the Health Council agreed to establish DECOS as a Committee of the Health Council. The membership of the Committee is given in Annex B.
The Committee

- R.A. Woutersen, *chairman*
  toxicologic pathologist, TNO Innovation for Life, Zeist; professor of translational toxicology, Wageningen University and Research Centre, Wageningen
- P.J. Boogaard
  toxicologist, Shell International BV, The Hague
- D.J.J. Heederik
  professor in risk assessment in occupational epidemiology, Institute for Risk Assessment Sciences, Utrecht University, Utrecht
- R. Houba
  occupational hygienist, Netherlands Expertise Centre for Occupational Respiratory Disorders (NECORD), Utrecht
- H. van Loveren
  professor of immunotoxicology, Maastricht University, Maastricht; National Institute for Public Health and the Environment, Bilthoven
- A.H. Piersma
  professor of reproductive and developmental toxicology, Utrecht University, Utrecht; National Institute for Public Health and the Environment, Bilthoven
- I.M.C.M. Rietjens
  professor of toxicology, Wageningen University and Research Centre, Wageningen
The Health Council and interests

Members of Health Council Committees are appointed in a personal capacity because of their special expertise in the matters to be addressed. Nonetheless, it is precisely because of this expertise that they may also have interests. This in itself does not necessarily present an obstacle for membership of a Health Council Committee. Transparency regarding possible conflicts of interest is nonetheless important, both for the chairperson and members of a Committee and for the President of the Health Council. On being invited to join a Committee, persons are asked to submit a form detailing the functions they hold and any other material and immaterial interests which could be relevant for the Committee’s work. It is the responsibility of the Health Council to assess whether or not someone can become a member. An expert who has no financial but another clearly definable interest, can become a member under the restriction that he will not be involved in the debate on the subject to which his interest relates. If a person’s interest is not clearly definable, he can sometimes be consulted as an expert. Experts working for a ministry or governmental organisation can be structurally consulted. During the inaugural meeting the declarations issued are discussed, so that all members of the Committee are aware of each other’s possible interests. For permanent Committees, possible conflicts of interest are considered for each topic of advice.
Annex

C

Comments on the public review draft

A draft of the present report was released in January 2016 for public review. The following organizations and persons have commented on the draft document:

- Lentz TJ, Park R, MacMahon K and Leonard SS, National Institute for Occupational Safety and Health (NIOSH), Cincinnati OH, USA
- Stremmelaar E, Vereniging Industrieel Oppervlaktebehandelend Nederland (ION), Nieuwegein
- van Broekhuizen P, Interfacultaire Vakgroep Milieukunde UvA BV, Amsterdam
- Sijbranda T, Coördinatiecentrum Expertise Arbeidsomstandigheden en Gezondheid (CEAG), Ministerie van Defensie, Doorn
- Paulussen E, Beek
### Water solubility of hexavalent chromium compounds

**Annex**

**Table 2** Water solubility of the best known hexavalent chromium compounds (based on IARC (1990) en de AGS (2014), modified by DECOS).^3^

<table>
<thead>
<tr>
<th>Compound</th>
<th>CAS number</th>
<th>Chemical formula</th>
<th>Water solubility (temperature)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ammonium chromate</td>
<td>7788-98-9</td>
<td>(NH₄)₂CrO₄</td>
<td>405 g/L (30 °C)</td>
</tr>
<tr>
<td>Ammonium dichromate</td>
<td>7789-09</td>
<td>(NH₄)₃Cr₂O₇ · 4H₂O</td>
<td>308 g/L (15 °C)</td>
</tr>
<tr>
<td>Barium chromate</td>
<td>10294-40-3</td>
<td>BaCrO₄</td>
<td>4.4 mg/L (28 °C)</td>
</tr>
<tr>
<td>Calcium chromate</td>
<td>13765-19-0</td>
<td>CaCrO₄</td>
<td>22.3 g/L (20 °C)</td>
</tr>
<tr>
<td>Calcium chromate dihydrate</td>
<td>8012-75-7</td>
<td>CaCrO₄ · 2H₂O</td>
<td>163 g/L (20 °C)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>182 g/L (45 °C)</td>
</tr>
<tr>
<td>Chromium trioxide</td>
<td>1333-82-0</td>
<td>CrO₃</td>
<td>625 g/L (20 °C)</td>
</tr>
<tr>
<td>Potassium chromate</td>
<td>7789-00-6</td>
<td>K₂CrO₄</td>
<td>629 g/L (20 °C), 792 g/L (100 °C)</td>
</tr>
<tr>
<td>Potassium dichromate</td>
<td>7778-50-9</td>
<td>K₂Cr₂O₇</td>
<td>49 g/L (0 °C)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1020 g/L (100 °C)</td>
</tr>
<tr>
<td>Lead chromate</td>
<td>7758-97-6</td>
<td>PbCrO₄</td>
<td>0.58 mg/L (25 °C)</td>
</tr>
<tr>
<td>Sodium chromate</td>
<td>7775-11-3</td>
<td>Na₂CrO₄</td>
<td>873 g/L (30 °C)</td>
</tr>
<tr>
<td>Sodium dichromate dihydrate</td>
<td>7789-12-0</td>
<td>Na₂Cr₂O₇ · 2H₂O</td>
<td>2300-2380 g/L (0 °C)</td>
</tr>
<tr>
<td>Nickel chromate</td>
<td>14721-18-7</td>
<td>NiCrO₄</td>
<td>Unsoluble</td>
</tr>
<tr>
<td>Strontium chromate</td>
<td>7789-06-2</td>
<td>SrCrO₄</td>
<td>1.2 g/l (0 °C), 30 g/l (100 °C)</td>
</tr>
<tr>
<td>Zinc chromate</td>
<td>13530-65-9</td>
<td>ZnCrO₄</td>
<td>Unsoluble</td>
</tr>
<tr>
<td>Zinc chromate hydroxide</td>
<td>15930-94-6</td>
<td>Zn₆CrO₄(OH)₂</td>
<td>Poorly soluble</td>
</tr>
<tr>
<td>Zinc potassium chromate</td>
<td>37300-23-5</td>
<td>KZn(CrO₄)₃</td>
<td>Unsoluble</td>
</tr>
<tr>
<td>Zinc potassium chromate hydroxide</td>
<td>11103-86-9</td>
<td>KZn(CrO₄)₃(OH)</td>
<td>0.5-1.5 g/L (20 °C)</td>
</tr>
</tbody>
</table>
Annex E

Carcinogenic classification of substances by the Committee

The Committee expresses its conclusions in the form of standard phrases:

<table>
<thead>
<tr>
<th>Category</th>
<th>Judgement of the Committee (GR\textsubscript{CIS})</th>
<th>Comparable with EU Category</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>67/548/EEC before 12/16/2008</td>
</tr>
</tbody>
</table>
| 1A       | The compound is known to be carcinogenic to humans.  
• It acts by a stochastic genotoxic mechanism.  
• It acts by a non-stochastic genotoxic mechanism.  
• It acts by a non-genotoxic mechanism.  
• Its potential genotoxicity has been insufficiently investigated. Therefore, it is unclear whether the compound is genotoxic. | 1 | 1A |
| 1B       | The compound is presumed to be carcinogenic to humans.  
• It acts by a stochastic genotoxic mechanism.  
• It acts by a non-stochastic genotoxic mechanism.  
• It acts by a non-genotoxic mechanism.  
• Its potential genotoxicity has been insufficiently investigated. Therefore, it is unclear whether the compound is genotoxic. | 2 | 1B |
| 2        | The compound is suspected to be carcinogenic to man. | 3 | 2 |
| (3)      | The available data are insufficient to evaluate the carcinogenic properties of the compound. | not applicable | not applicable |
| (4)      | The compound is probably not carcinogenic to man. | not applicable | not applicable |

Hexavalent chromium compounds
Health-based occupational cancer risk calculations

Heederik D. et al. Department of Environmental Epidemiology, Institute for Risk Assessment Sciences, Utrecht University, Utrecht.

Studies selected

Steenland et al. (1996) have published a meta-SMR for chromium VI exposure and lung cancer based on 10 different cohort studies. All studies had elevated SMR, indicative of a consistent elevated risk from chromium exposure. Some of the studies included did not have an exposure component, thus internal exposure response relations could not be derived for several of the studies included. This analysis has been used by SCOEL (2004) in a quantitative risk assessment by making a series of assumptions regarding exposure duration and level and confounding by smoking.

Seidler et al. (2013) performed a systematic literature review for studies that published exposure response relations for Chromium VI. They selected studies on risks for more than one cumulative exposure category (apart from controls) and had adjusted for cigarette smoking. Studies eligible for inclusion were reviewed by two individuals and SIGN scored for study quality (Scottish Intercollegiate Guidelines Network, 2008). Studies were classified to be of low quality when methodological weaknesses were expected to have affected the outcomes of a study. The high quality studies (SIGN scores ++ ) were used to
assess the exposure response relations. These studies fulfil most of the quality criteria and when not fulfilled the conclusions of the study or review are thought very unlikely to alter. Exposure-response relations were obtained by fitting linear models to the data using least square statistics weighted by the person years in each exposure category. Five studies originating from two cohorts of chromium exposure production workers were included. A study by Birk et al. (2006) was not used because Chromium VI levels were calculated on the basis of biomonitoring data. However, urinary chromium measurements cannot distinguish between Chromium III and Chromium VI exposure, because Chromium VI is reduced in the human body, introducing additional uncertainty.

The average slope from the two studies selected was used in the risk assessment by DECOS. Excess risk was calculated for a 40 year exposure, from age 20 to 60, and a latency period of 10 years. Excess risks of respectively 4 per 10,000 and 4 per 1,000 were observed at age 75 at a Chromium VI concentration of 0.1 µg/m³ and 1 µg/m³ using European mortality data.

Seidler et al. (2013) comment that the studies used for risk calculations do not distinguish mortality experience in workers exposed to soluble versus insoluble chromium. Thus, the risk calculations refer to both forms of Chromium VI. A differentiated evaluation of risk remains a future task.

Calculations (see Table 3)

For the purpose of the risk assessment by DECOS, calculations were redone using Dutch mortality data, and until the whole population died. Mortality has been calculated on the basis of mortality figures for lung cancer for five year age categories obtained from the Central Bureau of Statistics (www.cbs.nl, consulted on September 8, 2016) and the Integral Cancer centres (www.iknl.nl, consulted on September 8, 2016). Mortality figures for 2000 to 2010 have been used, by age and gender. Rates for males and females were used which implies that calculations result in population average risks. Mortality rates were smoothed to avoid large differences between age categories and modelled rates were used in the analysis. Rates (mortality per 100,000 person years) have been used in a survival analysis. Such an analysis can be conceptualized as two cohorts of equal size, followed from birth. For occupational exposures, exposure starts at age 20 and gradually builds up till age 60. The cohort gradually reduces in size because of lung cancer mortality and other causes of death. The cohorts are being followed till age 100. The first cohort is non-exposed, the second is exposed to
chromium resulting in an elevated mortality from chromium exposure. Calculations were performed with software from the R project for statistical computing (http://www.r-project.org/, consulted on September 8, 2016) under Windows.

The following exposures were obtained for a risk of 4 per 1,000 and 4 per 100,000 respectively: 4 per 1,000; 1.04 µg/m$^3$ and 4 per 100,000; 0.0104 µg/m$^3$.

These calculated exposure levels are very similar to the ones calculated by Seidler et al., despite the fact that these risks were calculated at a higher age (>100). The reason is that the expected higher risks, as calculated by DECOS, are compensated because of the lower (combined) male and female lung cancer rates instead of male lung cancer rates. Seidler et al. (2013) in their calculations used male rates only. If male lung cancer rates would have been used in these calculations by DECOS, resulting exposure levels would have been approximately 28% lower.

### Table 3

Occupational exposure levels at excess lung cancer risk of 40E-4 and 40E-6. Additional calculations based on the study by Seidler et al. (2013).

<table>
<thead>
<tr>
<th>Excess risk 40E-4</th>
<th>Occupational exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td># male rates age 75</td>
<td>1.398798 µg/m$^3$</td>
</tr>
<tr>
<td># male rates age end of cohort</td>
<td>0.7311646 µg/m$^3$</td>
</tr>
<tr>
<td># male + female rates age 75</td>
<td>1.84018 µg/m$^3$</td>
</tr>
<tr>
<td># male + female rates age end of cohort</td>
<td>1.038465 µg/m$^3$</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Excess risk 40E-6</th>
<th>Occupational exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td># male rates age 75</td>
<td>0.01395511 µg/m$^3$</td>
</tr>
<tr>
<td># male rates age end of cohort</td>
<td>0.00728933 µg/m$^3$</td>
</tr>
<tr>
<td># male + female rates age 75</td>
<td>0.01836072 µg/m$^3$</td>
</tr>
<tr>
<td># male + female rates age end of cohort</td>
<td>0.01036222 µg/m$^3$</td>
</tr>
</tbody>
</table>

### References (for Annex F)


Critical data used for the calculation of the health-based cancer risk values for hexavalent chromium compounds

DECOS evaluated the relevant experimental animal studies and human studies (till November 2015) in its meetings. DECOS observes that after the publication of its previous advice (DECOS, 1998) a limited number of animal studies and a significant number of human studies have been published.

DECOS evaluated the original literature on hexavalent chromium compounds in view of the recent reviews by IARC (2012), NIOSH (2013), NTP (2014), and especially in view of reviews by European organizations such as SCOEL (2004) and the AGS (2013). \(^{3,6,7,10,28}\)

For the present evaluation DECOS used the meta-analysis published by Seidler et al. (2013). In the Table (4) below from Seidler et al., a number of alternatives for the risk calculation are summarized. In addition, DECOS calculated a number of its own alternatives (see Paragraph 5.1 and Annex F).
Table 4  Excess lung cancer risk at 1 µg/m³ workplace Cr (VI) concentration for the male German population* applying the conditional or life-table methods. (Source: Seidler et al. Int Arch Occup Environ Health (2013) 86:943-955.)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>ß=1.75</td>
<td>ß=0.68</td>
<td>ß=2.82</td>
<td>ß=4.52</td>
</tr>
<tr>
<td>1</td>
<td>40 µg/m³ x years</td>
<td>Conditional (background mortality = 41/1,000)</td>
<td>74</td>
<td>2.9</td>
<td>1.1</td>
<td>4.6</td>
</tr>
<tr>
<td>1</td>
<td>40 µg/m³ x years</td>
<td>Life-table</td>
<td>74</td>
<td>2.3</td>
<td>0.9</td>
<td>3.7</td>
</tr>
<tr>
<td>1</td>
<td>40 µg/m³ x years</td>
<td>Life-table</td>
<td>80</td>
<td>3.2</td>
<td>1.2</td>
<td>5.2</td>
</tr>
<tr>
<td>1</td>
<td>40 µg/m³ x years</td>
<td>Life-table</td>
<td>89</td>
<td>4.1</td>
<td>1.6</td>
<td>6.5</td>
</tr>
<tr>
<td>1</td>
<td>40 µg/m³ x years</td>
<td>Conditional (background incidence = 70/1,000)</td>
<td>No age restriction</td>
<td>4.9</td>
<td>1.9</td>
<td>7.9</td>
</tr>
</tbody>
</table>

*Assuming a lung cancer mortality up to age 74 of 41/1,000

Assuming a lifetime risk of incidence lung cancer of 7 %
Innovation and the knowledge infrastructure
Before we can harvest knowledge in the field of healthcare, we first need to ensure that the right seeds are sown.

Healthy working conditions
How can employees be protected against working conditions that could harm their health?

Environmental health
Which environmental influences could have a positive or negative effect on health?

Healthy nutrition
Which foods promote good health and which carry certain health risks?

Prevention
Which forms of prevention can help realise significant health benefits?

Areas of activity
Optimum healthcare
What is the optimum result of cure and care in view of the risks and opportunities?

Innovation and the knowledge infrastructure
Before we can harvest knowledge in the field of healthcare, we first need to ensure that the right seeds are sown.

Hexavalent chromium compounds
Health-based recommendation on occupational exposure limits

Hexavalent chromium compounds
Health-based recommendation on occupational exposure limits

Advisory Reports
The Health Council’s task is to advise ministers and parliament on issues in the field of public health. Most of the advisory opinions that the Council produces every year are prepared at the request of one of the ministers.

In addition, the Health Council issues unsolicited advice that has an ‘alerting’ function. In some cases, such an alerting report leads to a minister requesting further advice on the subject.

Areas of activity
Optimum healthcare
What is the optimum result of cure and care in view of the risks and opportunities?

Prevention
Which forms of prevention can help realise significant health benefits?

Healthy nutrition
Which foods promote good health and which carry certain health risks?

Healthy working conditions
How can employees be protected against working conditions that could harm their health?

Environmental health
Which environmental influences could have a positive or negative effect on health?

Innovation and the knowledge infrastructure
Before we can harvest knowledge in the field of healthcare, we first need to ensure that the right seeds are sown.

Hexavalent chromium compounds
Health-based recommendation on occupational exposure limits