European Parliament

Protection of workers from exposure to carcinogens or mutagens: Third proposal

Detailed appraisal of the European Commission's impact assessment

STUDY

EPRS | European Parliamentary Research Service

Author: Stefano Vettorazzi
Ex-Ante Impact Assessment Unit
PE 627.144 – December 2018

EN

Protection of workers from exposure to carcinogens or mutagens: Third proposal

Detailed appraisal of the European Commission's impact assessment

FINAL

The European Commission proposal COM(2018) 171 final, adopted on 5 April 2018 and referred to Parliament's Committee on Employment and Social Affairs (EMPL), seeks to amend the Carcinogens and Mutagens Directive 2004/37/EC (CMD) by establishing binding occupational exposure limit values (OEL) for cadmium, beryllium, arsenic acid and its salts, formaldehyde, and 4.4'-methylene-bis(2-chloroaniline), the first three also including their respective inorganic compounds.

Following an initial appraisal by the European Parliamentary Research Service of the strengths and weaknesses of the European Commission's impact assessment (IA) accompanying the proposal, the EMPL Committee requested a more detailed and focused appraisal regarding the process and evidence base used for setting the limit values for cadmium and beryllium, as well as some of the limitations of the analysis performed in the IA.

This study illustrates how an initial set of values have been identified, selected for further assessment and subsequently chosen by the Commission.

As regards the evidence base used in the IA for setting the preferred OEL values, the study shows that the IA has relied on a vast amount of up-to-date information, making the overall analysis convincing and robust.

As regards the estimated number of workers exposed to cadmium and beryllium, the study concludes that the values considered by the external contractors of the Commission for their modelling appear to be plausible and justified, based on the availability of data. However, the full current and future disease burden deriving from historic exposures to cadmium and beryllium is not captured, a weakness that is acknowledged in the IA.

EPRS | European Parliamentary Research Service

AUTHOR

Stefano Vettorazzi, Ex-Ante Impact Assessment Unit

This paper has been drawn up by the Ex-ante Impact Assessment Unit of the Directorate for Impact Assessment and European Added Value, within the Directorate-General for Parliamentary Research Services (EPRS) of the Secretariat of the European Parliament.

To contact the Unit, please email: eprs-impactassessment@europarl.europa.eu

LINGUISTIC VERSIONS

Original: EN

Manuscript completed in November 2018.

DISCLAIMER AND COPYRIGHT

This document is prepared for, and addressed to, the Members and staff of the European Parliament as background material to assist them in their parliamentary work. The content of the document is the sole responsibility of its author(s) and any opinions expressed herein should not be taken to represent an official position of the Parliament.

Reproduction and translation for non-commercial purposes are authorised, provided the source is acknowledged and the European Parliament is given prior notice and sent a copy.

Brussels © European Union, 2018.

PE 627.144
ISBN: 978-92-846-3464-4
doi10.2861/890113
CAT: QA-06-18-276-EN-N

eprs@ep.europa.eu
http://www.eprs.ep.parl.union.eu (intranet)
http://www.europarl.europa.eu/thinktank (internet)
http://epthinktank.eu (blog)

Executive summary

On 5 April 2018, the European Commission adopted the proposal COM(2018) 171 final, seeking to amend the Carcinogens and Mutagens Directive 2004/37/EC (CMD) by establishing binding occupational exposure limit (OEL) values for five carcinogenic chemical agents. They include, inter alia, cadmium (Cd), beryllium (Be) and their respective inorganic compounds. This proposal was referred to the European Parliament's Committee on Employment and Social Affairs (EMPL).

As a follow-up to the initial appraisal[1] of the strengths and weaknesses of the European Commission's impact assessment (IA) accompanying this proposal, drawn up by the European Parliamentary Research Service's Ex-ante Impact Assessment Unit, the EMPL Committee requested on 15 October 2018 a more detailed and focused appraisal of the IA. This request concerned the process and evidence base used in the IA for setting the limit values for cadmium and beryllium, notably in light of some knowledge gaps and methodological challenges identified in the IA in relation to the number of workers exposed and the estimation of the burden of disease.

In providing the requested analysis, this detailed appraisal firstly examines the process by which the Commission identified an initial set of occupational exposure limit (OEL) values, and subsequently selected a few of them as the preferred options. Secondly, it assesses the overall evidence base on which those involved in the aforementioned process have based their analyses. Finally, it seeks to clarify some of the aforementioned methodological challenges and knowledge gaps acknowledged by the Commission in its IA. It does not attempt to deal with the substance of the proposal and the policy choices made.

Chapter 1 of this study introduces the analysis performed. Chapter 2 clarifies the scope of the analysis and the approach chosen. The scope reflects the request made by the EMPL Committee. Chapter 3 illustrates the overall process that the Commission followed in order to identify the OEL values retained for further assessment and, subsequently, to select the preferred values. To this end, the study details the process by which the Scientific Committee on Occupational Exposure Limits (SCOEL) first recommended or proposed occupational exposure limit, short-term limit and biomonitoring guidance values that the Advisory Committee on Safety and Health at work (ACSH) subsequently evaluated. Based on the findings of SCOEL and the ACSH, the external contractors engaged by the European Commission carried out a cost-benefit (CBA) and a multi-criteria analysis (MCA), considering an additional set of OEL reference values. In the light of the CBA and MCA performed by the external contractors, and of the comparison of the retained policy options against the standard Better Regulation Guidelines criteria of effectiveness, efficiency, and coherence, the IA concludes by selecting as preferred options the values proposed by the ACSH.

In the case of cadmium, the preferred value coincides with the value recommended by SCOEL. For beryllium, the IA selected as preferred option the OEL value proposed by the ACSH, while the SCOEL recommended an OEL value 10 times stricter. For cadmium, the preferred OEL value of 8-h TWA (8-hour time-weighted average) of 1 µg/m^3 (inhalable dust fraction) would be set after a transitional period of seven years, during which it would be fixed at the higher value of 8-h TWA 4 µg/m^3 (inhalable dust fraction).

However, the IA does not appear to have taken up the request of the ACSH to investigate whether the combined biomonitoring and TWA OEL approach could be included in the CMD. For beryllium, the preferred 8-h TWA OEL value of 0.2 µg/m^3 (inhalable dust fraction) would be set after a transitional period of five years, during which the higher 8-h TWA OEL value of 0.6 µg/m^3 (inhalable dust fraction) would be fixed. In addition, the Commission decided to include a notation for dermal

[1] Vettorazzi S., Protection of workers from exposure to carcinogens or mutagens: third proposal, initial appraisal of a Commission IA, EPRS, European Parliament, 2018.

and respiratory sensitisation. However, the IA does not takes up the ACSH proposal to set a biomonitoring guidance value (BGV) of 0.04 µg/l urine, as also recommended by SCOEL.

Chapter 3 of this study also examines the evidence base listed in the recommendations, opinions, and final reports of SCOEL, the ACSH, the external contractors and the European Commission to substantiate the respective analyses.

The analysis performed is not exhaustive because assessing each individual piece of evidence referenced would have required specific toxicological and epidemiological competences, which were not available in-house at the time of the request made by the EMPL Committee.

The alternative solution of assessing them in-house, by using internationally recognised metrics such as the journal impact factor, was also ruled out because it would have implied making the analysis available at a time not compatible with the deadline set by the EMPL Committee. As such, the present analysis is limited to assessing how recent the evidence listed is, as well as its nature (e.g. surveys, guidelines, scientific publications, etc.).

On the basis of the analysis carried out in this study regarding the references consulted by SCOEL, the ACSH, the external contractors and the Commission, it can be concluded that, overall, the Commission IA has been based, directly and indirectly, on a vast amount of relevant and up-to-date information. This includes, inter alia, papers, manuals, guidelines and surveys, published in scientific journals or by authoritative research centres and international organisations. The evidence base used provides a sound knowledge base for the analytical work carried out, which appears to be convincing and robust.

Chapter 4 of the study provides additional explanations on the methodological challenges and knowledge gaps specifically referred to in the EMPL Committee's request regarding in particular the disease burden and workers' exposure to cadmium and beryllium.

As regards the disease burden, the external contractors and the IA conclude that the burden of disease for cadmium, evaluated for two health endpoints (lung cancer and elevated proteinuria), may be underestimated. The same applies to the burden of disease for beryllium, evaluated for two health endpoints (cancer and chronic beryllium disease). The fact that only current uses of cadmium and beryllium are covered, and therefore only current exposures are considered in the analysis, and that not all health endpoints could be quantified and monetised, are among the reasons that explain the under-estimation of the disease burden.

As regards workers' exposure to cadmium, the two values considered by the external contractors for the modelling (10 000 and 30 000), and taken over in the IA, appear to be reasonable, based on the availability of data at national and EU level, and the way some of them were gathered. However, it is acknowledged that a larger exposed workforce results in an increase in both the costs and benefits. Their extent, as well as the relative magnitudes of the cost and benefit increases, depends on the assumptions made about the concentrations to which the additional workers are exposed.

Regarding workers exposure to beryllium, the IA's estimate of 54 071 workers exposed (excluding the construction sector) appears plausible, based on the comparison of the three methods used by the external contractors to estimate them. However, it is acknowledged that the greatest uncertainty is exposure distribution. According to the external contractors, should parts of the EU have higher exposure levels than implied by the survey chosen for the analysis, and closer to the US distribution, then the costs, and hence company closures, would be significant at all target OEL values. However, benefits would also be higher.

Table of contents

1. Introduction 1

1.1. Background 1

1.2. Structure of the study 2

2. Scope and approach of the analysis 3

2.1. Scope of the analysis 3

2.2. Approach chosen to perform the analysis 4

3. Process followed to set the preferred IA occupational exposure limit values 5

3.1. Scientific Committee on Occupational Exposure Limits 6

3.1.1. Description of the SCOEL 6

3.1.2. Identification of the proposed value for cadmium (SCOEL/OPIN/336) 6

3.1.3. Identification of the recommended value for beryllium (SCOEL/REC/175) 8

3.1.4. Evidence base 10

3.2. Advisory Committee on safety and health at work 12

3.2.1. Description of the ACSH 12

3.2.2. Identification of the proposed value for Cadmium (doc. 663/17) 13

3.2.3. Identification of the proposed value for beryllium (doc. 662/17) 14

3.2.4. Evidence base 15

3.3. Risk & Policy Analysts et al. 17

3.3.1. Identification of the values for cadmium acting as reference points 17

3.3.2. Identification of the values for beryllium acting as reference points 20

3.3.3. Evidence base 21

3.4. European Commission 23

3.4.1. Evidence base 25

4. Selected methodological challenges 27

4.1. Workers exposure to cadmium and beryllium ____ 27
4.1.1. Workers exposure to cadmium ____ 27
4.1.2. Workers exposure to beryllium ____ 29
4.2. Disease burden ____ 31
4.2.1. Disease burden estimated by RPA: cadmium ____ 32
4.2.2. Disease burden considered by the Commission: cadmium ____ 33
4.2.3. Disease burden estimated by RPA: beryllium ____ 34
4.2.4. Disease burden considered by the Commission ____ 36
Conclusions ____ 38
References ____ 40

Table of figures

Figure 1: simplified workflow of EU OEL setting under the Carcinogens and Mutagens Directive 2004/37/EC _____ 5

Table of tables

Table 1: references listed in opinion SCOEL/OPIN/336 _____ 10
Table 2: references listed in recommendation SCOEL/REC/175 _____ 11
Table 3: OEL values acting as reference points considered in the RPA study _____ 18
Table 4: summary of monetised costs and benefits _____ 19
Table 5: STEL reference levels considered in the RPA study _____ 20
Table 6: OEL reference levels considered in the RPA study _____ 20
Table 7: references listed in the RPA report on Cadmium _____ 21
Table 8: references listed in the RPA report for beryllium _____ 22
Table 9: range of policy options retained for assessment _____ 23
Table 10: workforce exposed to cadmium and cadmium compounds - published data _____ 27
Table 11: occupationally exposed population in the EU-28 _____ 28
Table 12: predicted employees affected by beryllium by sector _____ 30
Table 13: occupationally exposed population in the EU-28 _____ 30
Table 14: current burden of disease due to past exposure to cadmium _____ 33
Table 15: future burden of disease (baseline) for a constant workforce of 10 000 workers _____ 33
Table 16: future burden of disease (baseline) for a workforce of 10 000 workers and turnover _ 33
Table 17: baseline scenario over 60 years for cadmium and its inorganic compounds _____ 33
Table 18: current burden of disease (CBD) due to past exposure to Be _____ 35
Table 19: future burden of disease (CBD, baseline) - constant workforce _____ 36
Table 20: baseline scenario over 60 years for beryllium _____ 36

List of abbreviations and acronyms

ACRONYM	DESCRIPTION
ACSH	Advisory Committee on Safety and Health at Work
AGS	Ausschuss für Gefahrstoffe
B-Cd	Cadmium concentration in blood
Be	Beryllium
BeS	Beryllium sensitisation
BeST	Beryllium Science and Technology Association
BGV	Biological guidance value
BLV	Biological limit value
BOELV	Binding occupational exposure limit value
Cd	Cadmium
CAD	Chemical Agents Directive (98/24/EC)
CBA	Cost-benefits analysis
CBD	Chronic beryllium disease
CDB	Current disease burden
CKD	Chronic kidney disease
CMD	Carcinogens or Mutagens at Work Directive (2004/37/EC)
CMR	Carcinogenic, mutagenic or toxic to reproduction
DALY	Disability-adjusted life year
DNEL	Derived no effect level
DRR	Dose-response relationship
ECHA	European Chemicals Agency
EFSA	European Food Safety Authority
ERR	Exposure-risk relationship
ESRD	End stage renal disease
EU-OSHA	European Agency for Safety and Health at Work
FDB	Future disease burden
GFR	Glomerular filtration rate
IA	Impact assessment
IARC	International Agency for Research on Cancer
ICdA	International Cadmium Association

ACRONYM	DESCRIPTION
IFA	Institut für Arbeitsschutz der Deutschen gesetzlichen Unfallversicherung (Institute for occupational safety of the German social accident insurance)
IIAC	Industrial Injuries Advisory Council
INRS	Institut National de Recherche et de Sécurité (France)
IOM	Institute of Occupational Medicine
K-Cd	Cadmium concentration in kidney cortex
KEMI	Kemikalieinspektionen (Swedish chemicals agency)
LEV	Local exhaust ventilation
LFC	Lowest feasible concentration
LOAEC	Lowest observed adverse effect concentration
LOAEL	Lowest observed adverse effect level
LOD	Level of detection
LOQ	Limit of quantification
MCA	Multi-criteria analysis
MoA	Mode of action
MRL	Minimal risk level
MS	Member States
NACE	Nomenclature statistique des activités économiques dans la Communauté Européenne
NAIC	North American industry classification
NIOSH	National Institute for Occupational Safety and Health
NOAEC	No observed adverse effect concentration
NOAEL	No observed adverse effect level
OEL	Occupational exposure limit
OELs	Occupational exposure limit values
OPIN	Opinion
OSH	Occupational safety and health
OSHA	Occupational Safety and Health Administration (US)
PBT	Persistent, bioaccumulative and toxic
PEL	Permissible exposure limit
QALY	Quality adjusted life year
RAC	(ECHA) Committee for risk assessment
REACH	Registration, evaluation, authorisation and restriction of chemicals

ACRONYM	DESCRIPTION
REC	Recommendation
SCOEL	Scientific Committee on Occupational Exposure Limits
STEL	Short-term exposure limit
TWA	Time-weighted average
vPvB	Very persistent and very bioaccumulative
U-Cd	Cadmium concentration in urine
WEEE	Waste electrical & electronic equipment
WHO	World Health Organization
WTP	Willingness to pay

1. Introduction

1.1. Background

On 5 April 2018 the European Commission adopted a proposal, COM(2018) 171 final,[2] which seeks to amend the Carcinogens and Mutagens Directive 2004/37/EC (CMD) by establishing binding occupational exposure limit values (BOELVs)[3] for five carcinogenic chemical agents. These are cadmium, beryllium, arsenic acid and its salts, formaldehyde, and 4.4'-methylene-bis(2-chloroaniline), the first three including also their respective inorganic compounds within the scope of the CMD.

The current proposal is the third one adopted under the Juncker Commission, complementing those adopted on 13 May 2016[4] and on 10 January 2017[5] covering respectively thirteen and seven carcinogens, processes and process-generated substances (PGSs). It fulfils the requirement under Article 16 of the CMD that limit values be set in respect of all those carcinogens or mutagens for which it is possible, based on the available information, including scientific and technical data. It is also part of a new initiative, set out in COM(2017) 12 final, aiming to modernise the structure of the EU occupational safety and health (OSH) legislation and policy ('acquis').

The proposal follows a European Parliament resolution[6] highlighting the importance of protecting workers from carcinogens, mutagens and reprotoxic substances. The resolution also called on the Commission to propose a revision of the CMD based on scientific evidence, adding more binding occupational exposure limit values where necessary.

In addition, it follows the Employment, Social Policy, Health and Consumer Affairs (EPSCO) Council conclusions of 5 October 2015. These stressed that 'increasing the level of protection of workers against carcinogens, mutagens and any other hazardous chemical agents at the workplace is a major and urgent priority' and invited the Commission to 'consider improvements to the legislation on carcinogens and mutagens, by reviewing the existing binding occupational limit values and adding new ones, as appropriate, based on impact assessment and evidence'.

After being referred to the Parliament's Committee on Employment and Social Affairs (EMPL), and following an initial appraisal[7] by the EPRS of the strengths and weaknesses of the European Commission's impact assessment (IA), SWD(2018) 88 final accompanying the proposal, on

[2] See Scholz N., Limits on exposure to carcinogens and mutagens at work: Third proposal, EPRS, European Parliament, 2018.

[3] To simplify the text, the current and previous two impact assessments use the term 'occupational exposure level' (OEL) to refer to any occupational exposure limit (value). This term refers to the limit of the time-weighted average (TWA) of the concentration in the air within the breathing zone of a worker, measured or calculated in relation to a reference period of eight hours. This analysis will follow the same approach. For additional information regarding OELs see: Scientific Committee on Occupational Exposure Limits (SCOEL), Methodology for derivation of occupational exposure limits of chemical agents. The general decision-making framework of the Scientific Committee on Occupational Exposure Limits, DG EMPL, European Commission, December 2017.

[4] See Scholz N., Limits on exposure to carcinogens and mutagens at work, EPRS, European Parliament, 2018. For an initial appraisal of the impact assessment accompanyng the Commission proposal, see Georgescu A.A., Protection of workers from exposure to carcinogens or mutagens, EPRS, European Parliament, 2016.

[5] See Scholz N., Limits on exposure to carcinogens and mutagens at work: Second proposal, EPRS, European Parliament, 2017. For an initial appraisal of the impact assessment accompanying the Commission proposal, see Vettorazzi S., Protection of workers from exposure to carcinogens or mutagens: second proposal, EPRS, European Parliament, 2017.

[6] European Parliament resolution of 25 November 2015 on the EU Strategic Framework on Health and Safety at Work 2014-2020 (2015/2107(INI)).

[7] Vettorazzi S., Protection of workers from exposure to carcinogens or mutagens: third proposal, initial appraisal of a Commission IA, EPRS, European Parliament, 2018.

15 October 2018 the EMPL Committee requested a more detailed and focused appraisal regarding the process and evidence base used in the IA for setting the (limit) values for cadmium (Cd) and its inorganic compounds, and beryllium (Be) and its inorganic compounds. Throughout the analysis, whenever Cd and Be are mentioned, the inclusion of their inorganic compounds is implicitly assumed.

1.2. Structure of the study

The study is organised as follows:

- Chapter 2 illustrates the scope of the analysis, as well as the approach chosen to analyse the issues identified by the EMPL Committee as deserving a more detailed and focused appraisal;
- Chapter 3 illustrates the process which has enabled the Commission to identify the preferred OEL values for Cd and Be and examines the evidence base used;
- Chapter 4 provides clarifications regarding the methodological challenges specifically referred to in the EMPL Committee's request.

2. Scope and approach of the analysis

This chapter seeks to clarify the scope of the analysis illustrated in chapters 3 and 4 as well as the approach chosen to analyse the issues identified by the EMPL Committee as deserving a more detailed and focused appraisal.

2.1. Scope of the analysis

While the initial appraisal[8] by the EPRS of the IA accompanying the Commission proposal focused on assessing the IA's strengths and weaknesses, in light of the Commission's Better Regulation Guidelines, this analysis focuses on the process which has been used by the Commission in selecting the preferred OEL values for two, out of the five, carcinogens considered by the proposal, i.e. Cd and Be.

In addition, it focuses on the evidence base supporting the IA regarding the aforementioned chemicals. Finally, it aims at providing additional explanations regarding some gaps in knowledge regarding the workers' exposure to these substances, and the methodological challenges encountered in analysing the likely impacts of the policy options retained for further assessment. These are specified in the EMPL Committee's request, which refers explicitly to the content of the IA, namely:

- 'the data collected for this impact assessment estimates a number of 10 000 workers currently exposed to cadmium and its inorganic compounds. However, only limited extrapolation from the responses received to some of the sectors has been possible and some indications of exposure could not be confirmed' (IA, p. 5). Thus, according to the IA, exposure to Cd and its inorganic compounds varies within a range of 2 900 – 300 000 workers between different estimates;
- [for Be and inorganic beryllium compounds] Table 1 of the IA states (p. 5) that while the assessed number of workers exposed varies within a range of 14 000 – 74 000, 'depending on which of the three datasets is chosen', the figure of 54 000 workers exposed has been chosen by the IA as a basis;
- 'There are, however, significant challenges related to the presented analysis. First of all, the disease burden on workers is likely to be underestimated due to several limitations of the study. When considering the disease burden, only the most sensitive cancer endpoint and the most sensitive other adverse health effects have been considered. However, workers may develop additional types of cancer and diseases at higher exposure levels than the doses for the most sensitive endpoints. Those other cancers / adverse health effects, that will be prevented as well, could not be taken into account when calculating in particular the benefits of the proposed OELs, leading to an underestimation of the potential benefits. Furthermore, regarding occupational cancer, the available epidemiologic evidence is scarce and not always sufficiently robust, inevitably affecting the reliability of the derived estimates for the number of cancer registrations and deaths. It can therefore be difficult to establish a causal relationship between cancer cases and exposure to a specific carcinogen. Moreover, occupational cancers may develop decades after exposures – including during retirement – complicating the possibility of identifying a causal link. As a result, the health benefits presented in this report are likely to be underestimated. The 60 year-time frame of the assessment poses also a challenge of anticipating future industrial

[8] Vettorazzi S., Protection of workers from exposure to carcinogens or mutagens: third proposal, initial appraisal of a Commission IA, EPRS, European Parliament, 2018.

developments, technological progress, changes in work organisation, etc. It is difficult to predict future trends in the use of the substances under consideration and therefore in occupational exposures, and how these trends will impact the baseline. Similarly, the assessment of the impact on international competitiveness and innovation could only be based on consultations and the model assumptions of RPA (2018), but not substantiated with hard evidence. Finally, data on the number of workers exposed is generally scarce and unreliable, and data on the current exposure levels across EU Member States is not always available. Therefore, the baseline shows more modest figures than other recent studies that estimated past burdens of disease' (IA, p. 19).

2.2. Approach chosen to perform the analysis

The approach chosen for performing the analysis illustrated in this paper considers the issues identified by the EMPL Committee as requiring further clarification, indicated in the previous section. In order to identify how the IA has set the preferred OELs for Cd and Be, this analysis will illustrate the process by which an initial set of values have been identified by the Commission as policy options to be retained for further assessment. These have been based on the evaluations carried out by:

- the Scientific Committee on Occupational Exposure Limits (SCOEL);
- the Advisory Committee on Safety and Health at Work (ACSH), and
- the consortium of external contractors led by Risk & Policy Analysts (hereinafter RPA), which has received the mandate by the Commission DG EMPL to analyse the health, socio-economic, and environmental impacts related to the third amendment of the CMD.

In order to assess the evidence base used by the Commission, SCOEL, ACSH, and RPA this study will examine the references listed in their recommendations, opinions, and final reports to substantiate the respective analyses.

The analysis performed is not intended to be exhaustive because assessing each individual piece of evidence would have required specific toxicological and epidemiological competences, which were not available in-house at the time of the request made by the EMPL Committee, and it would have implied making the analysis available at a time not compatible with the deadline set by the EMPL Committee.

In order to provide clarifications regarding the methodological challenges specifically referred to in the EMPL Committee's request, this study will further analyse the explanations provided by SCOEL, ACSH, and RPA in their respective documents.

It is worth noting that the final report prepared by RPA et al.[9] was not available at the time of writing the initial appraisal of the IA accompanying the Commission proposal; it is still not publicly available at the time of writing this appraisal. The report has been provided by DG EMPL upon specific request of the Ex-Ante Impact Assessment Unit (IMPA), following the EMPL Committee's request. DG EMPL has authorised IMPA to quote some of its contents for the purpose of this analysis, subject to indicating that the RPA report is not published yet.

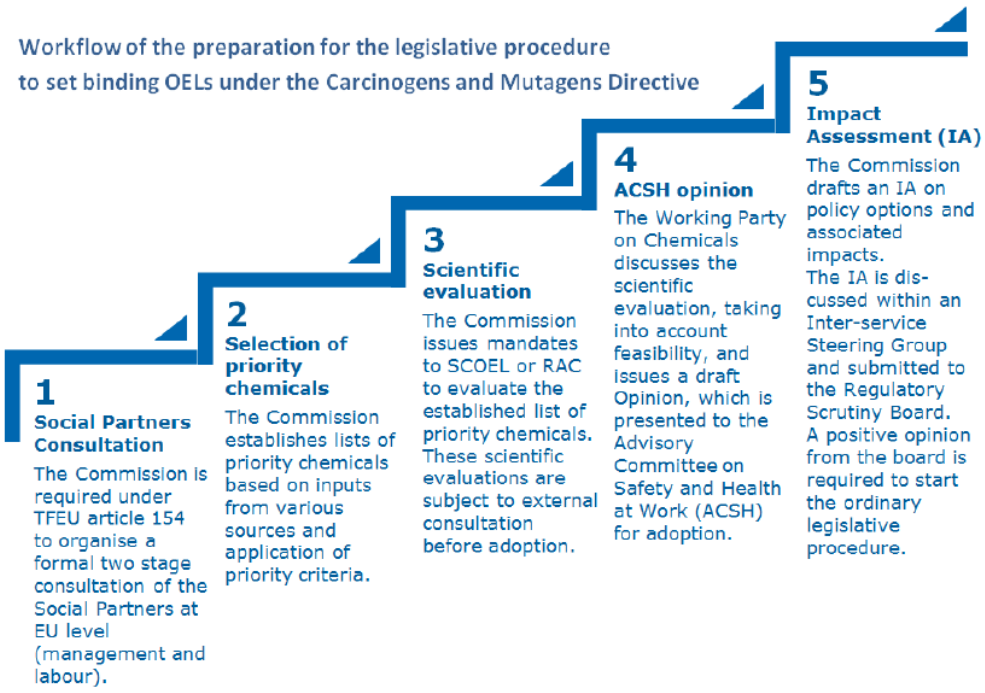
[9] Risk & Policy Analysts (RPA), Forschungs- und Beratungsinstitut Gefahrstoffe (FoBiG), COWI, and EPRD Office for Economic Policy and Regional Development (EPRD Biuro Polityki Gospodarczej i Rozwoju Regionalnego), Third study on collecting most recent information for a certain number of substances with the view to analyse the health, socio-economic and environmental impacts in connection with possible amendments of Directive 2004/37/EC, Final Report prepared for the European Commission, DG EMPL, Brussels, 8 February 2018. The report is not yet published.

3. Process followed to set the preferred IA occupational exposure limit values

This chapter seeks to illustrate the overall process which has led the Commission to identify the OEL values retained for further assessment and subsequently the preferred values; this is the same process which the Commission has followed in the first and second amendment of the CMD. To this end, it will illustrate the process by which an initial set of values have been separately identified by SCOEL, ACSH, and RPA and finally by the Commission in its IA.

The rationale for illustrating separately the processes followed by the aforementioned actors is effectively illustrated by referring to the following diagram, included in the Commission IA:

Figure 1: simplified workflow of EU OEL setting under the Carcinogens and Mutagens Directive 2004/37/EC



Source: IA (Figure 3, p. 14).

Steps 1 and 2 are outside the scope of this analysis, and therefore they will not be discussed.

Step 3 saw the involvement of SCOEL and RAC, the Committee for Risk Assessment of the European Chemicals Agency (ECHA). However, RAC was involved by the Commission in providing scientific advice regarding two chemical substances which are outside the scope of the current analysis, namely MOCA (4,4'-Methylene-bis(2-chloroaniline), and arsenic acid and its inorganic salts. As such, the description of the process by which OEL values were identified will regard only SCOEL.

Step 4 involved both the Working Party on Chemicals, and the ACSH.

As regards step 5, the IA states that in selecting its policy options, the Commission sought scientific advice from SCOEL, RAC and the ACSH (IA, p. 3), which adopted opinions for all five priority substances envisaged by the proposal. RPA worked on analysing the health, socio-economic, and environmental impacts of the policy options, considering the opinions and recommendations adopted by SCOEL and ACSH for setting some of the OEL reference values it analysed.

The following sections, therefore, will be aimed at clarifying how the Commission has identified the OEL values retained for further assessment, and how it selected the preferred ones, based on the independent contributions provided by SCOEL, the ACSH, and RPA.

3.1. Scientific Committee on Occupational Exposure Limits

3.1.1. Description of the SCOEL

The Scientific Committee on Occupational Exposure Limits (SCOEL) was set up on 3 March 2014 by Commission Decision 2014/113/EU, aligning its functioning with the Commission's rules on expert groups.

The Committee assists the Commission, in particular, in evaluating the latest available scientific data and in recommending occupational exposure limits for the protection of workers from chemical risks, to be set at Union level pursuant to Directive 98/24/EC (the chemical agents directive, CAD), and to the CMD. The definition of scientific data is provided in the CAD and CMD.

The Committee does this through the preparation of health-based scientific recommendations for the Commission (based on a pre-defined methodology) which are used to underpin regulatory initiatives on OEL values for chemicals in the workplace. During this procedure, draft recommendations from SCOEL undergo a stakeholder consultation to allow interested parties to submit comments and/or further data.

The 21 members of SCOEL for the 2015-2018 term of office have been selected following an open call for expression of interest, and have been appointed in their personal capacity by Commission Decision C(2015) 2369 final.

3.1.2. Identification of the proposed value for cadmium (SCOEL/OPIN/336)

On 12 December 2016 DG EMPL requested SCOEL to prepare a recommendation on OEL values and/or a scientific opinion regarding cadmium and its inorganic compounds and/or review its Recommendation SCOEL/SUM/136 regarding Cd, adopted in February 2010.

In 2010 SCOEL concluded by recommending an 8h-TWA (time-weighted average) OEL value of 4 µg/m^3 (respirable[10] dust fraction), based on non-cancer respiratory effects, in addition to a biological limit value (BLV) of 2 µg Cd/g creatinine in urine.[11]

On 8 February 2017, following the Commission request, SCOEL adopted Opinion SCOEL/OPIN/336. According to it, the [2010] value of 4 µg/m^3 'must be seen in close conjunction with the derived BLV, as both refer to and are protective for different toxicity endpoints of relevance (local and systemic).

[10] As regards the sampling methods, the RPA report on Be (p. 22) states that there are three different methods of measuring exposure, which need to be defined alongside an OEL value, namely:
- **inhalable**: particles inhaled though the mouth and nose, <100 µg;
- **respirable**: inhaled particles penetrating to the unciliated airways of the lung (alveolar region), <10 µg;
- **total particulate**: inhaled particles penetrating beyond the larynx, <30 µg (also known as thoracic, or total mass or total dust).

[11] In this regard, the author of this analysis would like to draw attention to a recent paper by Adams S.V. and Newcomb P.A. (2014) discussing the properties of concurrent measurements of cadmium concentration in urine and cadmium concentration in blood in relation to the duration and timing of a known exposure. See Adams S.V. and Newcomb P.A. (2014), Cadmium blood and urine concentrations as measures of exposure: NHANES 1999–2010. Journal of exposure science and environmental epidemiology 24(2):163-170.

Thus, implementation of both elements of the OEL- TWA and BLV- are of critical importance. An isolated OEL (8-h TWA) of 4 µg/m³ (not linked with a BLV) would [in fact] not appear being equally protective against the systemic nephrotoxicity of Cd' (p. 10).

This is the reason why, according to SCOEL (p. 10), 'an 8h-TWA OEL (not connected with biological monitoring) should be 1 µg/m³', based on the evaluations of published data (primarily by Thun et al., 1991[12]) carried out by WHO in 2000,[13] and by the German federal institute for occupational safety and health (BAuA) in 2014.[14] As such, **SCOEL proposes an 8-h TWA OEL value of 1 µg/m³ (inhalable dust fraction)**.[15] Of note, the issue regarding how to ensure protection against the systemic nephrotoxicity of Cd would be raised subsequently by the ACSH (see later).

However, the RPA report on cadmium, in referring to the SCOEL (2017) opinion, states that a value of 1 µg/m³ (inhalable dust fraction) corresponds implicitly to a *lower* respirable concentration. The RPA report goes on by referring to a 2013 report[16] of the Swedish competent authority mentioning a transformation factor of 2 to 2.5 to estimate a concentration for the respirable fraction from the data on the inhalable fraction (p. 9).

The RPA report concludes by stating that 'SCOEL (2017) implicitly provides a threshold of 0.4 µg/m³ for cadmium (respirable fraction) ... ' and that '... this transformation is important for the assessment of the carcinogenic potency (above threshold) as in this specific case, both epidemiological data and experimental animal data on local carcinogenicity (lung cancer), refer to the respirable fraction' (p. 9). As regards the impact of choosing a different conversion factor, see section 3.3.1 of this analysis.

In this regard, the plenary minutes of the meeting in Berlin on 8-10 February 2017 state that 'the REC-136 [the 2010 SCOEL Recommendation on Cd] was updated but was not adopted in the presented form by the members during the plenary. The predominant issue was that the set of OELs including the TWA and the BLV would require to be implemented together in order to serve the needs for protection of workers at the workplace. It was otherwise accepted that the airborne value(s) would be adjusted by a correspondingly appropriate additional uncertainty factor of

[12] Thun, M.J., Elinder, J.G., Friberg, L. (1991), Scientific basis for an occupational standard for cadmium. American Journal of Industrial Medicine 20(5):629–642.

[13] WHO (Word Health Organization), Air Quality Guidelines for Europe. WHO Regional Publications. European Series, No. 91, 2nd edition, WHO, Copenhagen, 2000. Individual chapters are also available for download on the WHO website.

[14] BAuA (Bundesanstalt für Arbeitsschutz und Arbeitsmedizin), Begründung zu ERB Cadmium in TRGS 910 [Technische Regel für Gefahrstoffe, Technical Rules for Hazardous Substances], BAuA, Dortmund/Berlin, 2014. However, its Annex 1 ('substance-specific values for carcinogenic substances classified as category 1A or 1B according to CLP Regulation or TRGS 905'), Table 1 ('list of substance-specific acceptable and tolerable concentrations'), indicates a tolerable value of 1 µg/m³ (inhalable fraction) (p. 18), while the Commission IA (Annex 5, Table 38, p. 87) indicates an OEL value of 1 µg/m³ (inhalable fraction) but only for non-carcinogenic effects. The aforementioned Table 38 specifies that a tolerable value in Germany is not regarded as a fixed OEL but as an upper limit, i.e. usually 4:1000 excess risk. However, exposures below the tolerable risk level but above the 'acceptable risk level' need to be minimised in order to avoid cancer risk. Of note, TRGS reflects the state of the art, the state of occupational health and occupational hygiene as well as other sound work-scientific knowledge relating to activities involving hazardous substances including their classification and labelling. The Committee on hazardous substances [Ausschuss für Gefahrstoffe, AGS] compiles or adapts the rules, and they are announced by the Federal Ministry of Labour and Social Affairs [Bundesministerium für Arbeit und Soziales, BMAS] in the Joint Ministerial Gazette [Gemeinsame Ministerialblatt, GMBl)' (TRGS 910, p. 1). The literature referenced by TRGS 910 is listed in its chapter 11 (pp. 139-154). For a diagram illustrating the derivation of an exposure-risk relationship (ERR), see Annex 3 of the TRGS 910 (p. 5).

[15] In its report on Cd, commenting on the 2017 SCOEL opinion, RPA states more precisely that 'in 2017 the lower OEL of 1 µg/m³ (inhalable fraction) was added in order to avoid both potential nephrotoxicity (or further systemic effects) and (systemic or local) carcinogenicity without the necessity to perform biological monitoring' (p. 9).

[16] Annex XV Report - Proposal for identification of a substance as a CMR [carcinogenic, mutagenic or toxic to reproduction] 1A or 1B, PBT [persistent, bioaccumulative and toxic], vPvB [very persistent and very bioaccumulative] or a substance of an equivalent level of concern, Substance Name: Cadmium Sulphide, EC Number: 215-147-8, CAS Number:1306-23-6.

minimum four as justified scientifically and in detail in the OPIN [SCOEL/OPIN/336] document' (Plenary meeting minutes SCOEL-100, p. 4).

SUMMARY OF SCOEL/OPIN/336 OPINION ON CADMIUM

SCOEL seems *initially* to suggest an 8-h TWA OEL value of 1 µg/m³ (inhalable dust fraction) coupled with a BLV of 2 µg Cd/g creatinine[17] in urine. This is, in fact, what can be read on page 7 summarising the decision taken before SCOEL starts illustrating the rationale for it.

However, *later* (p. 10), SCOEL proposes an 8-h TWA OEL value of 1 µg/m³ (inhalable dust fraction), not coupled with a BLV, which corresponds to Option 2 of the IA. The later appears to be the correct reading, based on the RPA report on Cd stating that in 2017 SCOEL proposed either a combination of an 8h-TWA OEL value of 4 µg/m³ (respirable dust fraction), coupled with a BLV of 2 µg Cd/g creatinine in urine, or an 8-h TWA OEL value of 1 µg/m³ (inhalable dust fraction) without BLV.

The 2017 opinion, however, does not provide any reasoning regarding the rationale for choosing the inhalable fraction as a reference point, instead of the respirable fraction of the 2010 recommendation. In addition, it does not clarify whether a conversion factor was used for converting measurements from respirable to inhalable.

3.1.3. Identification of the recommended value for beryllium (SCOEL/REC/175)

On 14 December 2015 DG EMPL requested SCOEL to prepare a recommendation on OEL values and/or a scientific opinion regarding beryllium and inorganic beryllium compounds.

Contrary to what was requested for Cd, in this case the Commission's mandate did not include the request to review Opinion SCOEL/OPIN/2015-175, which is only mentioned in the background section of the mandate. However, this opinion (referring to the United States occupational safety and health agency's proposal concerning Be) appears not to be available on the SCOEL section of the Commission's CIRCABC website, or on the internet.

On 8 February 2017, following the Commission request, SCOEL adopted Recommendation SCOEL/REC/175 proposing an 8h-TWA OEL value of 0.02 µg/m³ (inhalable dust fraction). According to SCOEL, the lung is the main target organ at inhalation exposure to Be, and at *relevant* exposure concentrations,[18] critical health effects include beryllium sensitization (BeS), chronic beryllium disease (CBD), in addition to carcinogenicity. BeS and CBD can also be caused by repeated exposure to low concentrations of Be (p. 7).

SCOEL states that recent studies have shown that individuals who are sensitised to BeS are considered to be at risk of developing subclinical and clinical CBD. As such, an OEL should protect from both these endpoints, as well as from carcinogenicity. According to the studies listed in Tables 8a (p. 33), and 8b (p. 34) of the recommendation, 'several cases of BeS have been observed at mean total dust levels around 0.1 µg/m³'. According to SCOEL, 'considering the severity of the effects, **an OEL of 0.02 µg/m³ for the inhalable dust fraction is recommended**' (p. 8).[19] Of note, the draft

[17] Creatinine is a breakdown product of creatine phosphate in muscle, and is usually produced at a fairly constant rate by the body. The SCOEL (2017) opinion states that 'the kidneys (and possibly bone) are the most sensitive target of systemic Cd toxicity following occupational exposure. Cd is a cumulative toxicant; the systemic manifestations associated with chronic exposure are related to the body burden of the element (liver and kidney content). Biological markers such as Cd-U (cadmium excretion in urine) allow the assessment of body burden, and to integrate all sources of Cd exposure, including contaminated food and smoking. The use of such biomarkers of exposure in most epidemiological studies conducted in occupational settings has allowed researchers to document reliable dose-effect/response relationship. A biological limit value will thus protect workers against systemic toxicity of Cd, mainly renal and bone effects' (p. 8).

[18] Based on the text contained in the document, it appears that by 'relevant' SCOEL is referring to concentrations > 1 000 µg/m³, which is regarded as a trigger level for acute beryllium disease (p. 40).

[19] According to SCOEL, 'this value also covers the NOAEC [no observed adverse effect concentration] for BeS and CBD of 0.02 µg respirable beryllium/m³ derived out of a human lifetime-weighted median exposure (Kelleher et al. 2001), which

recommendation of SCOEL was subject to a consultation period, during which several comments were submitted for consideration to SCOEL.[20]

In addition to long-term exposure, high short-term exposure may correlate with the development of CBD. According to SCOEL, based on the evaluation within the Madl A.K. et al. (2010) study[21] which revealed that beryllium-sensitised workers and those exerting CBD were exposed to concentrations higher than 0.2 µg/m³, **a short-term exposure limit** (STEL) **of 0.2 µg/m³** is proposed.[22]

According to SCOEL, however, the available data are not enough to allow a correlation to define a safe BLV, but studies have shown that the analytical measurement of Be in urine can be used as an indicator of current exposure to it. Based on the available data, SCOEL therefore recommends a **biological guidance value** (BGV) **of 0.04 µg/l urine** (p. 9).

Based on the analysis carried out, SCOEL concludes that it 'considers the available data basis sufficient for the recommendation of an OEL' (p. 42).

SUMMARY OF SCOEL/REC/175 RECOMMENDATION FOR BERYLLIUM

SCOEL recommends an OEL (8-h TWA) value of 0,02 µg/m³ (inhalable dust fraction); this value differs from the 8h-TWA OEL value of 0,2 µg/m³ (inhalable dust fraction) preferred by the Commission in its IA, which is the value agreed later on by the three interest groups represented within the ACSH.[23]

In addition, SCOEL proposes a short-term exposure limit of 0.2 µg/m³ and a biological guidance value of 0.04 µg/l urine.

Finally SCOEL recommends a notation for dermal and respiratory sensitisation.

is also supported by Schuler et al (2012) who reported a LOAEC [lowest observed adverse effect concentration] of 0.04 µg/m³ at an average concentration for the respirable fraction. A NOAEL [no observed adverse effect level] for the carcinogenic effects cannot be determined from the studies available. Since beryllium is not directly genotoxic and a synopsis of available data indicate that the described carcinogenic effects occurred at considerably higher concentrations, it can be assumed that this OEL will protect also from carcinogenic effects' (p. 8). See Kelleher P.C., Martyny J.W., Mroz M.M., Maier L.A., Ruttenber A.J., Young D.A., Newman L.S. (2001), Beryllium particulate exposure and disease relations in a beryllium machining plant. Journal of Occupational and Environmental Medicine 43(3):238-249, and Schuler C.R., Virji M.A., Deubner D.C., Stanton M.L., Stefaniak A.B., Day G.A., Park J.Y., Kent M.S., Sparks R., Kreiss K. (2012), Sensitization and chronic beryllium disease at a primary manufacturing facility, part 3: exposure-response among short-term workers. Scandinavian Journal of work, environment & health, 38(3):270-281.

[20] Among the comments submitted to SCOEL during the consultation period, available on the European Commission CIRCABC website of the SCOEL, a contribution submitted by the Beryllium science & technology association (BeST) discusses the plausibility of using BeS as a critical effect for setting an OEL.

[21] Madl A.K., Unice K., Brown J., Kolanz M.E., Kent M.S. (2007), Exposure-response analysis for beryllium sensitization and chronic beryllium disease among workers in a beryllium metal machining plant. Journal of Occupational and Environmental Hygiene 4(6):448-466.

[22] According to the SCOEL's methodology for derivation of occupational exposure limits of chemical agents, in fact, 'Where possible, SCOEL tries to develop health-based BLVs. These are based either on a direct relationship between a biomarker of exposure and an early reversible adverse health effect or, on a relationship between a biomarker of exposure and the chemical's IOEL or BOEL ... where the available data do not support a health-based BLV, like in the case of non-threshold carcinogens, SCOEL may establish a BGV' (p. 7).

[23] The Commission's preferred OEL value coincides with the (final) value that, according to the ACSH opinion adopted on 31 May 2017 (doc 662/17), was agreed by the three interest groups represented within it (employers, workers, and governmental). In addition, the ACSH opinion states that an 8h-TWA OEL value of 0,6 µg/m³ (inhalable fraction) was also agreed by the three IGs for a transitional period of 5 years; this value is represented by Option 4 of the Commission IA.

3.1.4. Evidence base

Evidence base for cadmium

The evidence base listed in opinion SCOEL/OPIN/336 is quite extensive, amounting to 194 references of which the majority is represented by scientific publications. These have not been checked against those included in the 2010 recommendation SCOEL/SUM/136 as this was outside the scope of the current analysis.

As already pointed out in the section describing the approach chosen in this appraisal, the analysis performed is not intended to be exhaustive because assessing each individual piece of evidence referenced would have required specific toxicological and epidemiological competences, which were not available in-house at the time of the request made by the EMPL Committee. In addition, it would have implied making the analysis available at a time not compatible with the deadline set by the EMPL Committee. As such, the conclusions drawn will be based on assessing how recent the various pieces of evidence listed are, as well as their nature (e.g. surveys, guidelines, scientific publications, etc.).

An in-house individual assessment based on some internationally recognised metrics used in the academic world, such as the journal impact factor[24] or the scimago journal rank,[25] to name but a few, was also ruled out because it would have been too time-consuming in light of the EMPL Committee's tight deadline.

The following table provides an overview of the references listed distributed according to their year of publication, grouped in discrete intervals for reasons that are self-evident.

Table 1: references listed in opinion SCOEL/OPIN/336

YEARS	ABSOLUTE VALUE	PERCENTAGE VALUE
1947-1980	26	13.4 %
1981-2000	96	49.5 %
2001-2017	72	37.1 %
Total	**194**	**100 %**

From the figures and percentages shown above, it can be concluded that the references listed in the 2017 SCOEL opinion are rather recent, as 37 % of them refer to the last 17 years. These include population-based health surveys, e.g. Åkesson et al. (2006),[26] guidelines, e.g. Lauwerys, R., Hoet, P. (2001),[27] and individual or collective scientific publications regarding several Cd-related aspects

[24] The journal impact factor (JIF), or impact factor (IF) of an academic journal, is a measure reflecting the yearly average number of citations to recent articles published in that journal. It is frequently used as a proxy for the relative importance of a journal within its field, as journals with higher impact factors are often deemed to be more important than those with lower ones. Impact factors are calculated yearly starting from 1975 for journals listed in the Journal Citation Reports.

[25] SCImago Journal Rank (SJR indicator) is a measure of scientific influence of scholarly journals that accounts for both the number of citations received by a journal and the importance or prestige of the journals where such citations come from. A journal's SJR is a numeric value indicating the average number of weighted citations received during a selected year per document published in that journal during the previous three years. Higher SJR values are meant to indicate greater journal prestige. The SJR indicator provides an alternative to the impact factor (IF) or average citations per document in a 2-year period.

[26] Åkesson A., Bjellerup, P., Lundh, T., Lidfeldt, J., Nerbrand, C., Samsioe, G. et al. (2006), Cadmium-induced effects on bone in a population-based study of women. Environmental Health Perspectives 114(6):830-834.

[27] Lauwerys, R., Hoet, P., Cadmium, in Industrial chemical exposure guidelines for biological monitoring, pp. 54-69. Lewis Publishers, Boca Raton, 2001.

such as cancer mortality, exposure, toxicity as well as documents published by world-class research institutions or international organisations (e.g. IOM, IARC, WHO, etc.).

Given that this opinion also provides a review of the most recent literature contained in its 2010 recommendation, as requested in the Commission 2016's mandate, it can be concluded that the evidence base used by SCOEL appears to be robust enough to support its opinion.

This conclusion appears to be supported also by SCOEL' statement that 'the core database relevant for grouping of Cd as a carcinogen and for OEL setting (8h-TWA and BLV) has not significantly changed since the time of the SCOEL Recommendation in 2010' (p. 7).

Evidence base for beryllium

The evidence base listed in recommendation REC/175 is also quite abundant, amounting to 128 references of which the majority is represented by scientific publications. As already pointed out above for Cd, the analysis performed has not assessed each individual piece of evidence. The following table provides an overview of the references listed distributed according to their year of publication, grouped in discrete intervals.

Table 2: references listed in recommendation SCOEL/REC/175

YEARS	ABSOLUTE VALUE	PERCENTAGE VALUE
1945-1980	3	2.3 %
1981-2000	17	13.3 %
2001-2017	108	84.4 %
Total	**128**	**100 %**

From the figures and percentages shown above, it can be concluded that the references listed in the 2017 SCOEL recommendation are even more recent than those used for the opinion on Cd, as about 85 % of them have been published or made publicly available on the internet during the last 6 years. These include, inter-alia, a cross-sectional survey (Deubner D. et al., 2001),[28] manuals (e.g. NIOSH, 2007),[29] monographs (IARC, 1993),[30] evaluations of the toxicological and epidemiological literature (e.g. Hollins D.M., 2009),[31] and individual or collective papers regarding Be-related issues.

[28] Deubner D., Kelsh M., Shum M., Maier L., Kent M., Lau E. (2001), Beryllium sensitization, chronic beryllium disease, and exposures at a beryllium mining and extraction facility. Applied Occupational and Environmental Hygiene 16(5):579–592.

[29] National Institute for Occupational Safety and Health (2007), NIOSH manual of analytical methods (NMAM) fifth edition. Beryllium in Air by Field-Portable Fluorometry. Method 7704.

[30] International Agency for Research on Cancer (1993), Beryllium, Cadmium, Mercury, and exposures in the glass manufacture. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans Volume 58, IARC, Lyon, 1993.

[31] Hollins D.M., McKinley M.A., Williams C., Winam A., Filos D., Chapman P.S., Madl A.K. (2009), Beryllium and lung cancer: a weight of evidence evaluation of the toxicological and epidemiological literature. Critical Reviews in Toxicology 39(sup 1):1-32.

SCOEL states (p. 6) that its evaluation is mainly based on the following sources ATSDR (2002),[32] WHO (2001[33], 2009[34]), US EPA (2008)[35], OSHA (2015),[36] Greim H. (2005),[37] and JRC (2012),[38] as well as on a literature update covering the 2002-2015 period (p. 6).

In addition, SCOEL states that several reviews regarding workplace exposure to Be and its compounds are available and have been consulted, such as IOM (2011),[39] NTP (2005),[40] Strupp C. (2011),[41] of which the IOM one reflecting in detail the current situation in Europe (p. 19).

Based on what is included in this recommendation, the evidence base used by SCOEL appears to be solid enough to support it.

3.2. Advisory Committee on safety and health at work

3.2.1. Description of the ACSH

The ACSH is a tripartite body set up in 2003 by Council Decision 2003/C218/01 to streamline the consultation process in the field of occupational safety and health (OSH), and rationalise the bodies created in this area by previous Council Decisions.[42]

The Committee's remit is to assist the European Commission in the preparation, implementation and evaluation of activities in the fields of safety and health at work.

The Committee is composed of three full members per Member State,[43] representing national governments, trade unions and employers' organisations, which are organised in three separate interest groups (IGs) within the Committee.

---

[32] Agency for toxic substances and disease registry (ATSDR), Toxicological profile for beryllium, U.S. Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry, Atlanta, USA, 2002.

[33] World Health Organization (WHO), Concise international chemical assessment document 32: beryllium and beryllium compounds, WHO, Geneva, 2001.

[34] World Health Organization (WHO), Beryllium in drinking-water: background document for development of WHO guidelines for grinking-water quality, WHO, Geneva, 2009.

[35] US EPA (2008), IRIS Toxicological review of beryllium and compounds. US Environmental Protection Agency, Washington, DC, 2008.

[36] OSHA, Occupational Safety and Health Administration (2015). Occupational exposure to beryllium and beryllium compounds. Federal register 80 (152): 47565-47828.

[37] Greim H. (ed) (2005), Beryllium and its inorganic compounds, The MAK-Collection for Occupational Health and Safety, Part I: MAK Value Documentations, Vol. 21. DFG, Deutsche Forschungsgemeinschaft, Wiley-VCH, Weinheim, Germany.

[38] JRC, Joint Research Centre (2012). Criteria Document for the Scientific Committee on Occupational Exposure Limits (SCOEL). Beryllium and beryllium compounds. Final report. September 2012.

[39] Institute of occupational medicine (IOM), Health, socio-economic and environmental aspects of possible amendments to the EU Directive on the protection of workers from the risks related to exposure to carcinogens and mutagens at work Beryllium and beryllium compounds, IOM Research Project: P937/4, Final Report, May 2011.

[40] National Toxicology Program (NTP), 11th Report on carcinogens, January 30, 2005, U.S. Department of Health and Human Services, NC, USA, 2005. The 14th Report on carcinogens, on 3 November 3 2016, is available on the NTP website. The individual profile for Be is also available for download, as well as the individual profile for Cd.

[41] Strupp C. (2011), Beryllium metal II. A review of the available toxicity data. The Annals of Occupational Hygiene, 55(1): 43–56.

[42] Namely, the former Advisory Committee on safety, hygiene and health protection at work, established by Council Decision 74/325/EEC, and the Mines safety and health Commission for safety and health in the coal mining and the other extractive industries (established originally as Mines Safety and Health Commission by a Council Decision of 9 and 10 May 1957), established by Council Decision 74/326/EEC.

[43] The members (and alternate members) of the ACSH for the period 29 February 2016-28 February 2019 have been appointed by the Council on 24 February 2016 (2016/C 079/01).

The Committee meets twice a year in a plenary configuration, chaired by the Commission. Its activities are coordinated by a 'Bureau', composed of two representatives from the Commission and the spokespersons and coordinators designated by the interest groups.

Working parties of experts supports the ACSH on given topics of interest, according to mandates agreed by the plenary Committee. These working parties are also tripartite but usually with smaller selected expert membership.

The ACSH working party on chemicals (WPC) undertakes broader chemicals policy support for the ACSH and Commission, and in particular detailed technical and policy negotiation of EU limit values. According to its 2017-2020 mandate, the WPC has, inter alia, the specific task of discussing the recommendations and opinions prepared by SCOEL for chemical substances.[44]

3.2.2. Identification of the proposed value for Cadmium (doc. 663/17)

The three IGs discussed Cd at the 21-22 March 2017 meeting of the WGC, during which a consensus on the following two approaches was reached (meeting minutes Doc.343-18, p. 8):

1. an OEL at 1 µg/m^3 (inhalable dust fraction) with a transitional period of 7 years (to end no later than 2027) at 4 µg/m^3 (inhalable dust fraction).
2. a combination of biomonitoring (0,02 µg/g creatinine in urine) and OEL;

With regard to the first approach, 'due to still unresolved uncertainties in the correct interpretation of the meaning of SCOEL opinion SCOEL/OPIN/336 concerning nephrotoxicity', the workers IG 'suggested the Commission to seek clarifications from SCOEL whether compliance with both the recommended biomonitoring value of 2 µg Cd/g creatinine in urine and an 8-h TWA of 4 µg/m^3 (respirable dust fraction) [SCOEL/SUM/136] would be protective against nephrotoxicity, or whether compliance with both the recommended biomonitoring value of 2 µg Cd/g creatinine in urine and an 8-h TWA of 4 µg/m^3 (inhalable dust fraction) is needed to achieve protection against nephrotoxicity' (meeting minutes Doc.343-18, p. 8).

During its 28th plenary meeting held in Luxembourg on 31 May 2017, the WGC presented, inter alia, the opinion regarding Cd (Doc. 663/17). The aforementioned approach one was confirmed. Approach two was agreed as being the combination of an airborne OEL with the biological monitoring value proposed by SCOEL 'which could be used as a mean of demonstrating control of workers' exposure in those Member States where biomonitoring is carried out. This would be based on complying with both the SCOEL biomonitoring value of 2 µg Cd/g creatinine in urine and the 8-h TWA of 4 µg/m^3 (respirable dust fraction) as recommended by SCOEL/OPIN/336 (p. 10 paragraph 2)' (Doc. 663/17, p. 1).

The ACSH agreed that both approaches present adequate technical means of protecting workers' health and requested the Commission to 'investigate whether the combined biomonitoring and TWA OEL approach could be included in the CMD'. Of note are the following observations made by the employers IG (Doc. 663/17, p. 1):

- 'should (the OEL-only based) approach 1 be the only approach retained by the regulators, it will require a fundamental change to the risk management strategy implemented by the H&S [health and safety] Departments and Occupational Doctors of the Cd-using industry, along with the redesign and commissioning of more

[44] According to the mandate 2017-2020 adopted on 30 November 2016 (Doc.1818/16), the working group Chemicals at the workplace established by the ACSH has, inter alia, the specific task of discussing 'the recommendations and opinions prepared by SCOEL for chemical substances as an approach to reducing and controlling exposure to workers, both for substances where limits can be set on the basis of health effects only and for substances where other factors also have to be considered (e.g. genotoxic carcinogens and/or technical feasibility issues) with the aim to prepare an opinion on them, as appropriate' (mandate 2017-2020, p. 2).

complex air cleaning systems, whilst not providing the safety net that approach 2 ensures thanks to the use of the urinary Cd BLV';

- 'the authors of the Jarüp study (1988),[45] which is key in developing the OEL proposal of 1 µg Cd/m³ (inhalable fraction), state (p. 228) that data " (…) indeed suggests that the cumulative blood cadmium dose is a more sensitive predictor of renal damage than cadmium in air, particularly at low levels of air cadmium concentrations", hence giving clear preference of the use of an exposure biomarker over an OEL for the prevention of systemic adverse effects'.

The workers IG observed, inter alia (Doc. 663/17, p. 1), that 'based on the ERR [Exposure-risk relationship] derived in Germany, an 8-hour exposure concentration of 4 µg/m³ Cd is associated with an additional cancer risk of 1:100. Should option 2 be implemented, the workers IG believes that this BOEL should be reviewed in due time with a view to lowering it to a value of not higher than 1.6 µg/m³ Cd (respirable) which is supposed to correspond to an additional cancer risk of 4:1,000)'.

SUMMARY OF ACSH DOC. 663/17 OPINION ON CADMIUM

The ACSH agreed on the following two approaches, both presenting 'adequate technical means of protecting workers' health', namely:

1. an 8h-TWA OEL at 1 µg/m³ (inhalable dust fraction) with a transitional period of 7 years (to end no later than 2027) at 4 µg/m³ (inhalable dust fraction);
2. an 8h-TWA OEL value of 4 µg/m³ (respirable dust fraction), coupled with a BLV of 2 µg Cd/g creatinine in urine.

The OEL value of approach 1 corresponds to Option 2 in the IA, while its transitional period value corresponds to Option 3 in the IA.

Of note, the ACSH approach 1 envisages a transitional period which SCOEL did not recommend in OPIN/336

3.2.3. Identification of the proposed value for beryllium (doc. 662/17)

The three IGs discussed Be at the 21-22 March 2017 meeting of the WGC, including recommendation SCOEL/REC/175. A draft opinion was agreed, proposing (meeting minutes Doc.343-18, p. 8):

- an 8h-TWA OEL value at 200 ng/m³ with an 8h-TWA OEL value at 600 ng/m³ for a transitional period of 5 years;
- notations for skin and respiratory sensitisation;
- the need for a footnote in the future annex III [of the CMD] recalling that biomonitoring of Be is particularly important for managing the risk of exposure.

During its 28th plenary meeting held in Luxembourg on 31 May 2017, the WGC presented, inter alia, the opinion regarding Be (Doc. 662/17). The values agreed by all three IGs were the following:

- an 8h-TWA OEL value at 200 ng/m³ [i.e. 0.2 µg/m³] with an 8h-TWA OEL value at 600 ng/m³ [i.e. 0.6 µg/m³] for a transitional period of 5 years. These two values correspond to Options 1 and 2 of the IA, respectively.
- a biological [guidance] value of 0.04 µg beryllium/l urine as recommended by SCOEL, with the ACSH suggesting that the OEL in Annex III of the CMD should include a

[45] The reference list contained in the SCOEL/OPIN/336 includes several studies carried out by Jarüp alone, while all the referenced studies carried out by Jarüp et al. have been published in other years. As such, and due to time constraints, it has not been possible to clarify to which study SCOEL refers to.

footnote to indicate the importance of biomonitoring for beryllium exposure risk management;[46]

- a notation for dermal and respiratory sensitisation as recommended by SCOEL.

Of note are the following observations made by the employers, and workers IGs, respectively (Doc. 662/17, pp. 2-3):

- 'the agreed value of 200 ng/m³ is protective against CBD[chronic beryllium disease], which is the recognised adverse health effect of concern to be considered for establishing OEL for Be. However, this value is not in line with available dose-response recent studies which identify a no-observed adverse effect level (NOAEL) at a higher level. In terms of technical feasibility, 200 ng/m³ is a very challenging target; industry refers to 600 ng/m³ in inhalable fraction (corresponding to the value recently adopted in USA of 200 ng/m³ in thoracic or total fraction, CFC sampling method) as the recommended exposure guideline in its voluntary product stewardship program to prevent the risk of CBD. Socio-economic impacts must be considered when adopting a BOEL. The employer IG requests that assessment conducted by RPA on the technical and economic feasibility of the adoption of BOELs for Be should be fully taken into consideration';
- 'as the agreed value of 200 ng/m³ is not protective against Be sensitisation (BeS) (cf. SCOEL/REC/175, the BOEL should be reviewed in due time with a view to lowering it to the value of 20 ng/m³ (inhalable fraction) recommended by SCOEL … to be protective against BeS'.

SUMMARY OF ACSH DOC. 662/17 OPINION ON BERYLLIUM

The ACSH agreed on the following:

- an 8h-TWA OEL value at 200 ng/m³ [i.e. 0.2 µg/m³] (inhalable dust fraction) with an 8h-TWA OEL value at 600 ng/m³ [i.e. 0.6 µg/m³] (inhalable dust fraction) for a transitional period of 5 years. These two values correspond to Options 3 and 4 of the IA, respectively.
- a biological guidance value of 0.04 µg beryllium/l urine, as recommended by SCOEL, with the ACSH suggesting that the OEL in Annex III of the CMD should include a footnote to indicate the importance of biomonitoring for beryllium exposure risk management;
- a notation for dermal and respiratory sensitisation as recommended by SCOEL.

Of note, for its part, SCOEL proposed an 8h-TWA OEL value at 0.02 µg/m³ (inhalable dust fraction) without transitional period. In addition, SCOEL proposed a short term exposure limit (STEL) of 0.2 µg/m³

3.2.4. Evidence base

Evidence base for cadmium

In ACSH's document DOC. 663/17, three specific comments were made by the employers IG (EIG).

[46] 'Human biomonitoring can be an effective tool for assessing exposure to a variety of chemicals as biomonitoring data integrates all routes (inhalation, dermal and oral) and sources of exposure (i.e. including occupational, environmental and lifestyle factors) ... but it does not provide information on individual routes of exposure. This is because biomonitoring generally makes an assessment of the exposure by quantitating a biomarker of exposure in blood, urine or other biological media. Thus, it is difficult to make an informed decision on an individual route of exposure. If available, additional information concerning the primary sources, routes of exposure and temporal variability will help inform sampling strategies, interpret the health implications of the data and provide the basic information for advice to limit exposure, if necessary'. Scott M.A., Angerer J., Boogaard P.J., Hughes M.F., O'Lone R.B., Robison S.H, Schnatter A.R., (2013), The use of biomonitoring data in exposure and human health risk assessment: benzene case study. Critical Review in Toxicology, 43(2):119–153 (pp. 120-121).

Comment (ii) states that 'should (the OEL-only based) approach ONE (1) be the only approach retained by the regulators, it will require a fundamental change to the risk management strategy implemented by the H&S Departments and Occupational Doctors of the Cd-using industry, along with the redesign and commissioning of more complex air cleaning systems, whilst not providing the safety net that approach TWO (2) ensures thanks to the use of the urinary Cd BLV. Indeed, urinary Cd [U-Cd], is first a comprehensive exposure bio-marker in the sense that it integrates all routes of uptake (ingestion and inhalation) ' (p. 2).

The EIG then adds that U-Cd is also a well-demonstrated predictor of kidney tubular damage, quoting a work by Chaumont et al. (2014). This piece of work is not mentioned either in the 2017 opinion SCOEL/OPIN/336 or in the 2010 recommendation SCOEL/SUM/136. Reference to it is not provided in the ACSH's opinion, but desk research appears to have identified it as a 2013 paper.[47]

Based on this paper, the EIG states that the fact that U-Cd is a comprehensive exposure bio-marker, and also a well-demonstrated predictor of kidney tubular damage, 'is a strong benefit for a cumulative toxicant such as Cd in two very different situations: in a systematic way, and in accidental situations.[48]

In comment (iii), the EIG refers to a Jarüp (1998)[49] study 'to highlight the fact that the authors of the study, which is key in developing the OEL proposal of 1 µg Cd/m^3 (inhalable fraction), state (p. 228) that data "(…) indeed suggests that the cumulative blood cadmium dose is a more sensitive predictor of renal damage than cadmium in air, particularly at low levels of air cadmium concentrations", hence giving clear preference of the use of an exposure biomarker over an OEL for the prevention of systemic adverse effects'.

No other references are mentioned in the ACSH's opinion; however, they appear to the ACSH convincing enough to support its request to the Commission 'to investigate whether the combined

[47] In their paper, the authors concluded that their study shows that 'the curvilinear relationship between U-Cd and K-Cd [Cd concentration in kidney cortex] described in industrial workers and assumed in recent models does not hold for the entire general population with a low environmental exposure to Cd. Over a lifetime, U-Cd shows age-related variations that appear to be largely determined by recent Cd intake and by the renal handling of proteins, particularly LMW [low molecular weight] proteins. These findings are particularly relevant for epidemiological studies of health risks associated with low environmental exposures to Cd. Observations in these studies based on U-Cd would be substantiated by the use of cumulative intake indicators that are unlikely to be confounded by recent Cd exposure and physiological variations in renal elimination of the metal. Various indicators might be used for that purpose based on, for instance, residence time in the studied area, consumption of locally produced foods, or Cd dietary intake estimated from food contamination data'. See Chaumont A., Voisin C., Deumer G., Haufroid V., Annesi-Maesano I., Roels H., et al. (2013), Associations of urinary cadmium with age and urinary proteins: further evidence of physiological variations unrelated to metal accumulation and toxicity. Environmental Health Perspectives 121(9):1047–1053. A reply to comments to their study made by Adam S.V. and Newcomb P.A. was provided on the following issue of the same journal by Chaumont A. and Bernard A.C. (2013), Urinary Cadmium as a Marker of Exposure in Epidemiological Studies: Bernard and Chaumont Respond. Environmental Health Perspectives 121(10):A296–A297, in which the authors concludes that they 'agree with Adams and Newcomb that there is no better way to assess individual exposure to Cd than by measuring the metal directly in urine or in blood. However, the question is whether one can reliably assess the long-term effects of low-level environmental Cd by means of a biomarker that reflects mostly recent exposure. A cautious interpretation of data is also needed because U-Cd is physiologically linked to proteinuria and albuminuria (Akerstrom et al. 2013), which are well-known predictors of bone and cardiovascular diseases (Barzilay et al. 2013; Smink et al. 2012)'.

[48] Namely: 'in a systematic way for plants where workplace air quality is well controlled, the involuntary ingestion route becomes the predominant uptake route over the inhalation route (it is worth noting that with the 2010 SCOEL recommendation of 4µg/m^3 respirable, involuntary ingestion is a significant part of the uptake). Involuntary ingestion cannot be controlled by compliance with an OEL; in accidental situations, when an air cleaning equipment malfunction goes undetected for some amount of time, the biomarker value acts as a safety net'.

[49] In reality, in SCOEL/OPIN/336 two 1998 works by Jarüp et al. are mentioned, namely: Järup, L., Bellander, T., Hogstedt, C., Spang, G. (1998a), Mortality and cancer incidence in Swedish battery workers exposed to cadmium and nickel. Occupational & Environmental Medicine 55(11):755-759, and Järup, L., Berglund, M., Elinder, C.G., Nordberg, G., Vahter, M. (1998b), Health effects of cadmium exposure - a review of the literature and a risk estimate. Scandinavian Journal of Work, Environment & Health 24(Supp 1):1-51.

biomonitoring and TWA OEL approach could be included in the CMD as a directly related provision', which is the ACSH's approach two, i.e. 'to combine an airborne OEL with the biological monitoring value proposed by SCOEL which could be used as a mean of demonstrating control of workers' exposure in those Member States where biomonitoring is carried out. This would be based on complying with both the SCOEL biomonitoring value of 2 µg Cd/g creatinine in urine and the 8 hour TWA of 4 µg/m^3 (respirable fraction) as recommended by SCOEL/OPIN/336 (page 10 paragraph 2, adopted 8th of February 2017)'.[50]

Evidence base for beryllium

In ACSH's document DOC. 662/17 no reference is mentioned or quoted.

3.3. Risk & Policy Analysts et al.

In 2017 DG EMPL requested RPA to assess the impacts of a range of OEL values for five chemical agents including, inter alia, Cd and Be. An additional objective of the study was the collection of information regarding the different OEL-deriving systems in EU Member States and selected third countries. A final objective, associated with the stakeholder consultation, was the collection of data and information feeding into the assessment of the OEL-deriving systems and the potential impacts of the OEL values. This included the collection of data and information on the extent of occupational exposure and the potential impacts of such OEL values by means of questionnaires, interviews, and site visits.[51]

On 8 February 2018, following the Commission request, RPA completed the final report,[52] the contents of which are extensively used in the IA for supporting the overall analysis and for identifiyng the OEL values retained for further assessment, as well as those selected as the preferred options. The report has been provided by DG EMPL upon specific request of IMPA, following the EMPL Committee's request. DG EMPL has authorised IMPA to quote some of its contents for the purpose of this analysis, subject to indicating that it is not yet publicly available. The two following sections describe how the OEL values for Cd and Be were identified by RPA.

3.3.1. Identification of the values for cadmium acting as reference points

As regards the study scope, the RPA report states that 'the assessment … is based on the assumption that only an OELV would be introduced and it would not be accompanied by a BLV' (p. 17). This approach appears to be consistent with the text contained in the SCOEL opinion (p. 10), where it proposes an 8-h TWA OEL value of 1 µg/m^3 (inhalable fraction), not coupled with a BLV.

In addition, RPA states that 'the objective of the study is to provide a comparison of the costs and benefits for a range of potential OELVs (as opposed to one or several specific OELVs). This range starts at the lowest technically feasible limit[53] and ends at the current OELs and encompasses the

[50] As regards the preference of using an exposure biomarker over an OEL, the author of this analysis would like to bring attention to a recent paper by Adams S.V. and Newcomb P.A. (2014) discussing an issue which does not appear to have been analysed by SCOEL, i.e. the properties of concurrent measurements of U-Cd and blood Cd (B-Cd) in relation to the duration and timing of a known exposure. See: Adams S.V. and Newcomb P.A. (2014), Cadmium blood and urine concentrations as measures of exposure: NHANES 1999–2010. Journal of exposure science and environmental epidemiology 24(2):163-170.

[51] See IA, Annex 4 (pp. 80-82).

[52] RPA et at. (2018), Third study on collecting most recent information for a certain number of substances with the view to analyse the health, socio-economic and environmental impacts in connection with possible amendments of Directive 2004/37/EC, Final Report prepared for the European Commission, DG EMPL, Brussels, 8 February 2018. The report is not published yet.

[53] In this regard, RPA invites to consider the discussion on the feasibility of an 8h-TWA OEL at 1 µg/m^3 (inhalable dust fraction) which is included in the report.

value in the SCOEL and ACSH opinions. Specific values have, however, been established for the purposes of the consultation exercise to provide reference points to the consultees who may otherwise have found it impossible to provide data on the costs of the measures being considered. The reference points used for cadmium are summarised [in the table] below' (p. 23).

Table 3: OEL values acting as reference points considered in the RPA study

Option	Respirable fraction (µg/m³)	Inhalable fraction (µg/m³)
SCOEL/OPIN/336 & ACSH Doc. 663/17	*0.4 µg/m³*	1 µg/m³
ACSH Doc. 663/17 (transition period)	*1.6 µg/m³*	4 µg/m³
REACH DNEL[37] & ICdA Guidance	4 µg/m³	*10 µg/m³*
Lowest national OEL (BE, IE, PL, ES)	2 µg/m³	*5 µg/m³*
Mean, median, and mode of current national OELs	10 µg/m³	*25 µg/m³*
Notes: Values in italics in shaded cells denote calculations by the study team using a Respirable->Inhalable conversion factor of 2.5. Where there are several OEL values in a Member State, the lower value was used for the calculation of mean, median and mode. Where particle size for Cd OEL has not been specified, it has assumed (for the purposes of calculating the mean, median and mode) that this is respirable since those Member States that specify the particle size of their OEL more often use 'respirable'.		

Legend: DNEL = Derived no effect level for substances
ICdA = International Cd Association

Source: RPA, Table 2-7 (p. 24)

As indicated above, RPA has used a factor of 2.5 for converting respirable to inhalable measurements (i.e. respirable x 2.5 = inhalable). According to RPA, this is a conservative estimate which has been chosen to ensure that the assessment is protective of the workers. However, the real-life conversion factor can be highly variable. Some stakeholders believe that the generic conversion factor should be 5 or 6, with 4 believed to be the average value by some industry sources consulted. At the same time the report acknowledges that 'although the establishment of a general factor is highly uncertain, such a factor is necessary for the purposes of this study, which needs to bring together data and suggestions expressed as different particle sizes' (p. 24).

The report states that the international cadmium association (ICdA) industry guidance document refers to the REACH DNEL [derived no effect level] of 4 µg/m³ respirable, corresponding to 10 µg/m³ inhalable using a conversion factor of 2.5 which is taken forward by RPA for its analysis. However, when conversion factors of 5 or 6 are used, 4 µg/m³ respirable would correspond to 20 µg/m³ or 25 µg/m³ inhalable.

The report states that other conversion factors have been considered within the framework of the sensitivity analysis in order to ensure that the compliance costs to industry are not underestimated. According to RPA, this has been necessary when estimating compliance costs for companies members of the iCdA which, in line with recommendation SCOEL/SUM/136, for a number of years have been measuring air concentrations as respirable fraction. The report states that using a conversion factor of 2.5 to generate a theoretical inhalable value could result in an underestimation of the true compliance costs to industry, while a higher 'real life' conversion factor would mean that more companies would not be in compliance with the potential OEL value if compared to the OEL value estimated based on a factor of 2.5 (p. 24).

Based on the aforementioned OEL values used as reference points, RPA assessed the total number of exposed workers, the current and future burden of disease (expressed in number of cases of lung

cancers and increased proteinuria[54] over 40 and 60 years), the benefits from avoided ill health, and the economic impacts of introducing a new OEL. Finally, RPA carried out both a cost-benefit analysis (CBA), and a multi-criteria analysis (MCA) for the different OEL reference values set at the outset.

The report regarding Cd concludes that 'due to the large number of uncertainties surrounding the estimates, the costs and benefits in the CBA and MCA should only be taken as an indication of the order of magnitude of the potential impacts of the OELVs. Therefore, the conclusion should go beyond a simple comparison of the costs and the benefits that could be monetised in this study and should consider all the information presented in this report, including the impacts that could not be monetised and the limitations and uncertainties of the analysis'.

Having clarified this, according to RPA the costs and benefits that could be monetised are summarised in the following table:

Table 4: summary of monetised costs and benefits

Reference OELV	PV benefits* over 60 years (€2017 million)	PV costs over 60 years (€2017 million)
25 µg/m³ (inhalable fraction)	(0.9-) 2–6	4 (179)
10 µg/m³ (inhalable fraction)	(4-) 8–34	14 or 44 (591)
5 µg/m³ (inhalable fraction)	(5-) 12–58	71 or 116 (711)
4 µg/m³ (inhalable fraction)	(6-) 13–64	79 or 116 (735)
1 µg/m³ (inhalable fraction)	(7-) 14–66	448 (758)
Monetised costs and benefits	Avoided lung cancer and elevated proteinurea cases vis-à-vis the baseline	RMMs Discontinuation of business** Transposition costs Measurements
Significant non-monetised costs and benefits	Simplification of rules for companies operating in several Member States	
Notes: Values in italics denote Respirable->Inhalable conversions on the basis of a factor of 2.5. *Values in brackets relate to sensitivity analysis using Cd-U DRR, lowest value of all scenarios. **Some methods (e.g. extrapolation from Cap Ingelec (2017) do not include these costs).		

Legend: RMMs = risk management measures PV = present value Source: RPA, Table 10-4 (p. 140)

According to RPA, bearing in mind that the benefits could not be monetised for some health endpoints, it can be concluded that the lowest OEL reference value at which the monetised benefits are likely to exceed the costs is around 10 µg/m³ (inhalable fraction), i.e. 4 µg/m³ (respirable fraction).

[54] Proteinuria, protein in urine, may indicate damage to the kidneys. RPA states that this endpoint covers a range of effects including (p. 70):

- elevated proteinuria, which is regarded as first sign of (tubular) kidney damage by SCOEL (and others);
- chronic kidney disease (CKD), which is defined by KDIGO (kidney disease improving global outcomes) as abnormalities of kidney structure or function, present for more than 3 months, with implications for health. CKD is classified based on cause, GFR category (glomerular filtration rate , volume of ultrafiltrate formed in the kidney tubules from the blood passing through the glomerular capillaries divided by time of filtration), and CGA staging [identify cause of CKD (C), assign GFR category (G), Assign albuminuria category (A)]. See Kidney Disease Improving Global Outcomes (2013), KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney International 3(2):1-150.
- end stage renal disease (ESRD) is the last stage of CKD and may require dialysis or a kidney transplant.

3.3.2. Identification of the values for beryllium acting as reference points

As regards the study scope, the RPA report states that the assessment concerns 'the impacts surrounding the setting of an OELV and STEL [short-term exposure limit] for Be' while 'the BGV is not investigated' (p. 9).

As already done for the analysis regarding Cd, RPA identifies several reference levels for OEL and STEL values to carry out a CBA, which are illustrated in the following table:

Table 5: STEL reference levels considered in the RPA study

Level	Reason for inclusion
0.2 µg/m^3 (inhalable)	STEL at the level proposed in SCOEL REC 175
0.4 µg/m^3 (inhalable)	Lowest current national STEL in EU Member States (Finland). Assumed inhalable since OEL is inhalable
5.77 µg/m^3 (inhalable)	Mean of current national STELs in EU Member States
8 µg/m^3 (inhalable)	Median of current national STELs in EU Member States
Source: RPA, see Table 3-1 for current STELs in Member States	

Source: RPA, Table 2-10 (p. 21)

Table 6: OEL reference levels considered in the RPA study

Level	Reason for inclusion
0.02 µg/m^3 (inhalable)	OEL at the level proposed in SCOEL REC 175
0.05 µg/m^3 (inhalable)	Intermediate level
0.1 µg/m^3 (inhalable)	Lowest current national OEL in EU Member States (Finland)
0.2 µg/m^3 (inhalable)	ACSH recommendation for OEL
0.35 µg/m^3 (inhalable)	Intermediate level
0.6 µg/m^3 (inhalable)	Equivalent to the USA PEL of 0.2 µg/m^3 (total particulate). Several respondents believe this is the lowest economically viable level.
1 µg/m^3 (inhalable)	Intermediate level
2 µg/m^3 (inhalable)	Median and mode of national OELs in EU Member States
Source: RPA, see Table 3-1 for current OELs in Member States	

Legend: PEL = Permissible exposure limit

Source: RPA, Table 2-9 (p. 20)

RPA states that all the OSHA (Occupational Safety and Health Administration) exposure values taken from the United States Department of Labor (2015) and used in the analysis have been multiplied by 2 to equate them to the inhalable values used in the EU.[55]

As done before for Cd, based on the aforementioned OEL reference levels, RPA assessed the total number of exposed workers, the current and future burden of disease (expressed in number of cases of chronic beryllium disease – CBD and cancer over 40 and 60 years), the benefits from avoided ill

[55] RPA states that there are different views regarding the use of a conversion factor between total particulate and inhalable results. The report acknowledges that 'SCOEL (2017) does not agree with having a conversion factor, but the study team believes it is essential as the inhalable sampling gives higher readings than total particulate sampling' (p. 23). In addition, RPA states that research by Kock H. et al., (2015) derived a value of 2.88, and that an assessment by AGS [Committee on Hazardous Substances] in Germany to set their OEL used a conversion factor of 2. For Be, a conversion factor of 2 was used by RPA. If a conversion factor of 2.88 or 3 had been used, RPA estimates that the costs and benefits would have both increased by about 50%. If a conversion factor of 1 had been used, RPA estimates that the costs and benefits would have both decreased by about 50%. According to RPA, the effect would be overall neutral (p. 145). See Kock H., Civic T., Koch W. (2015), Beryllium concentrations at European workplaces: comparison of 'total' and inhalable particulate measurements. Annals of occupational hygiene 59(6):788-796.

health, and the economic impacts of introducing a new OEL. Finally, RPA carried out both a CBA, and an MCA for the different OEL reference levels.

The report states that no avoided cases of cancer are predicted for the proposed OEL values 'as the levels required to cause it (>10 µg/m^3) are well above those at which companies across the EU are currently operating' (p. 82), adding the SCOEL/REC/175 conclusion that 'the recommended OEL is not based on carcinogenicity and is considerably lower as compared to exposure estimates leading to lung cancer in humans'. As such, the CBA and MCA express the current and future disease burden only as the number of cases of CBD.

RPA concludes its analysis by recommending what follows (p. 155):

- 'overall, RPA believes that the breakeven point for an OEL value for Be is between 0.2 and 0.6 µg/m^3 (inhalable). For the reasons outlined in the sensitivity and multi-criteria analyses, RPA believes that an OEL value between 0.4 and 0.6 µg/m^3 (inhalable) may better reflect the breakeven point'. RPA states that 'this is similar to the 2017 recommendation of the ACSH WGC of an OEL value of 0.2 µg/m^3 (inhalable) with a value of 0.6 µg/m^3 (inhalable) during a transitional period of 5 years';
- RPA also recommends 'a transition period with an initial OEL value between 0.6 µg/m^3 (inhalable) and 1 µg/m^3 (inhalable). In addition, RPA recommends that the OEL value is reassessed after a few years of the transition period to ensure that the industry has found ways of achieving the final value and analysis methods with limits of quantification down to 10% of the final OEL value are available';
- finally, RPA states that further primary research, monitoring exposure levels, would be required to investigate whether there is an issue with Be in construction. According to RPA, it seems likely that any exposure to Be occurs in specific construction processes and it is important to identify exactly which these are.

3.3.3. Evidence base

Evidence base for cadmium

The evidence base listed in the RPA report on Cd amounts to 83 different pieces of work, including the opinion and recommendation adopted by SCOEL in 2010 and 2017, and by the ACSH. Some of these references have also been quoted by SCOEL, but a check on the degree of overlap has not been carried out due to time constraints.

The following table provides an overview of the references listed distributed according to their year of publication, grouped as usual in discrete intervals.

Table 7: references listed in the RPA report on Cadmium

YEARS	ABSOLUTE VALUE	PERCENTAGE VALUE
1947-1980	2	2.4 %
1981-2000	18	21.7 %
2001-2017	63	75.9 %
Total	**83**	**100 %**

From the figures and percentages shown above, it can be concluded that the references listed in the RPA report on Cd are, in percentage value, more recent than those listed in the SCOEL 2017 opinion, as those published in the last seven years are equal to 76 % against a 37 % value.

Among the references quoted in the RPA report, we can find a report on a model to estimate the costs of exposed people to Cd (Cap Ingelec, 2017),[56] a meta-analysis prepared by EFSA (European Food Safety Agency) regarding the dose-effect relationship of Cd (EFSA, 2009),[57] documentation by the American Conference of governmental industrial hygienists on the threshold limit values and biological exposure indices (ACGIH, 2001),[58] a systematic review on breast cancer frequency and exposure to Cd (Rahim F. et al., 2013),[59] a paper on occupational cancer burden in Great Britain (Rushton L. et al., 2012)[60] to quote just a few of them.

Based on the references listed, it can be concluded that the evidence listed in the RPA report appears to be very up-to-date, providing a sound knowledge base for the analytical work carried out that, it is worth stressing, was focused on performing an impact analysis starting from a set of OEL reference values, rather than identifying a recommended or suggested OEL value to be set at EU level, as was the mandate assigned by the Commission to SCOEL and the ACSH.

Evidence base for beryllium

The evidence base listed in the RPA report on be amounts to 109 different pieces of work, including the recommendation and opinion adopted by SCOEL and the ACSH in 2017, respectively. Some of these references have also been quoted by SCOEL, but a check on the degree of overlap has not been carried out due to time constraints.

The following table provides an overview of the references listed distributed according to their year of publication, grouped as usual in discrete intervals.

Table 8: references listed in the RPA report for beryllium

YEARS	ABSOLUTE VALUE	PERCENTAGE VALUE
1945-1980	15	13.8 %
1981-2000	8	7.3 %
2001-2017	86	78.9 %
Total	**109**	**100 %**

From the figures and percentages shown above, it can be concluded that the references listed in the RPA report on Be are, in percentage value, slightly less recent than those listed in the SCOEL 2017 opinion, as those published in the last seven years consulted by RPA are equal to a percentage value of 79 % against an 84.4 % value for SCOEL.

Among the references quoted in the RPA report, we can find a review of the epidemiological evidence regarding occupational exposure to Be and cancer risk (Boffetta P. et al., 2012),[61] an EPA

[56] Cap Ingelec (2017), Cadmium Industrial Users - Creation of a model to estimate the costs of exposed people protection upgrade, Report for the International Cadmium Association (ICdA), I-IM17014-11DD, 22 December 2017.

[57] European Food Safety Authority (2009), Meta-analysis of dose-effect relationship of Cadmium for benchmark dose evaluation, EFSA Journal, Parma, 31 March 2009.

[58] American Conference of Governmental Industrial Hygienists (2001), Cadmium and compounds in: Documentation of the threshold limit values and biological exposure indices, 7th edition, ACGIH, Cincinnati, 2011.

[59] Rahim F., Jalali A., Tangestani R., (2013), Breast cancer frequency and exposure to cadmium: a meta-analysis and systematic review, Asian Pacific Journal of Cancer Prevention, 14(7):4283-4287.

[60] Rushton L. et al., (2012), Occupational cancer burden in Great Britain, British Journal of Cancer, 107(Suppl. 1):S3-7.

[61] Boffetta P., Fryzek J.P., Mandel J.S. (2012), Occupational exposure to beryllium and cancer risk: a review of the epidemiologic evidence. Critical Reviews in Toxicology 42(2):107-118. EPA Environmental Protection Agency (2008): Toxicological Review of Beryllium and Compounds. April 1998: Draft Revised May, 2008. In Support of Summary Information on the Integrated Risk Information System (IRIS) U.S. Environmental Protection Agency, Washington DC.

toxicological review of Be and its compounds (EPA, 1998)[62], a cohort mortality study of workers at Be processing plants (Schubaue-Berigan M.K. et al., 2011)[63], a cohort mortality study on lung cancer incidence among patients with Be disease (Steenland K., Ward E., 1991),[64] to quote just a few of them.

From the analysis carried out, it appears that, as for Cd, also for Be the references included in the RPA report provide a sound knowledge base for the analytical work carried out in performing an impact analysis starting from a set of OEL reference values.

3.4. European Commission

The following table illustrates the different policy options considered in the Commission IA and, in grey, the preferred OEL values.

Table 9: range of policy options retained for assessment

OPTION	DESCRIPTION	CADMIUM	BERYLLIUM	DECISION
1	Baseline: no EU binding OEL values (BOELV)			R
2	Lowest EU OEL value (#)	1 µg/m³ (+)	0.1 µg/m³	RfA
3	Intermediate EU OEL value (#)	4 µg/m³	0.2 µg/m³ (*)	RfA
4	Highest EU OEL value (#)	10 µg/m³	0.6 µg/m³	RfA

Legend: # = 8-hour time weighted average (TWA) exposure
+ = this preferred option includes a transitional period of 7 years at the level of option 3
* = this preferred option includes a transitional period of 5 years at the level of option 4
R = Retained RfA = Retained for Assessment

Source: author, based on IA (Table 4, p. 5)

Based on SCOEL, ACSH, and RPA opinions, recommendations, and reports it can be concluded that the OEL values (inhalable fraction) retained for further assessment in the IA are based on the following sources:

SUMMARY OF EUROPEAN COMMISSION'S IA

OPTION	CADMIUM	SOURCE	BERYLLIUM	SOURCE
2	1 µg/m³	SCOEL/OPIN/336 ACSH Opinion (Doc. 663/17)	0.1 µg/m³	RPA (lowest current national OEL in Finland)
3	4 µg/m³	ACSH Opinion (Doc. 663/17) transition period	0.2 µg/m³	ACSH Opinion (Doc. 662/17)
4	10 µg/m³	REACH DNEL & ICdA Guidance (*)	0.6 µg/m³	ACSH Opinion (Doc. 662/17) transition period

* The value has been obtained by RPA applying a respirable->inhalable conversion factor of 2.5.

Legend: DNEL = Derived no effect level for substances ICdA = International Cd Association

Source: author, based on RPA reports on Cd and Be

[62] Environmental Protection Agency (EPA), Toxicological review of Beryllium and compounds. EPA, Washington DC, April 1998.

[63] Schubauer-Berigan M.K., Couch J.R., Petersen M.R., Carreón T., Jin Y., Deddens J.A. (2011), Cohort mortality study of workers at seven beryllium processing plants: update and associations with cumulative and maximum exposure. Occupational and Environmental Medicine, 68(5):345-353.

[64] Steenland K., Ward E. (1991), Lung cancer incidence among patients with beryllium disease: a cohort mortality study. Journal of the National Cancer Institute 83(19):1380-1385.

As regards Cd, although the preferred option corresponds to one of the two approaches agreed at the March 2017 meeting of the WGC by the three interest groups represented within the ACSH, and to the value recommended by SCOEL, the Commission IA appears to not have taken up the request of the ACSH to 'investigate whether the combined biomonitoring and TWA OEL approach could be included in the CMD' (Doc. 663/17, p. 1).

However, the IA states, without further explanation, that 'regarding the options proposed referring to biological monitoring or binding biological limit values; it has to be kept in mind that it is currently legally not possible to establish such limit values under the CMD' (IA, p. 57).

As regards Be, the three interest groups represented within the ACSH agreed on an OEL value of 0.2 µg/m^3, which is different from the 0.02 µg/m^3 value recommended by SCOEL. In this regard the employers IG observed that while the agreed value is protective against CBD, it is not in line with available dose-response recent studies which identify a no-observed adverse effect level at a higher level. In addition, the agreed value is a very challenging target.

On the other hand, the workers IG observed that as the agreed value is not protective against BeS, the OEL should be reviewed with a view to lowering it to the value of the 0.02 µg/m^3 value recommended by SCOEL (inhalable fraction) in order to be protective against BeS.

In addition, the three interest groups represented within the ACSH agreed on the biological guidance value of 0.04 µg beryllium/l urine as recommended by SCOEL, with the ACSH suggesting that the OEL in Annex III of the CMD should include a footnote to indicate the importance of biomonitoring for beryllium exposure risk management.

The Commission IA, in selecting the preferred option for Be, has not taken up the SCOEL recommendation regarding the recommended OEL value, deciding to adopt the ACSH agreed value, which was supported by the RPA analysis. However, the Commission does not appear to have taken up both the SCOEL and the ACSH recommendation and suggestion, respectively, to include a biological guidance value of 0.04 µg beryllium/l urine.[65]

Of note, in explaining the scope of its study, RPA stated that the assessment regarding the impacts surrounding the setting of an OEL and STEL values for Be did not include the issue of a biological guidance value. As such, it is reasonable to assume that this issue was not included in the Commission's mandate to RPA.

In analysing the impact of the aforementioned policy options for Cd and Be, the IA refers to its Tables 6 and 9 (IA, p. 22, pp. 25-26), showing the results of the MCA carried out by RPA, to state that the compliance and administrative costs for companies represent the largest cost burden across all three options both for Cd and Be.

Compliance costs have been defined by RPA (p. 88) as the additional costs of complying with an OEL value, i.e. the costs incurred by companies in bringing down their exposure to levels below the set OEL value.

According to RPA, the total compliance cost of the introduction of an OEL value depends on the number of companies above the OEL value and the cost for each company of reducing the exposure concentration to a level below that value. In turn, the costs for each company depend on the size of the relevant activities (e.g. number of moulding machines, number of workers, etc.) and the gap between the actual exposure and the OEL value, as well as on the type of risk management measure

[65] On the issue of biomonitoring Be in urine, the author of this analysis would like to mention a recent and voluminous paper written by Paul R. et al. (2017), as it is not included in the SCOEL recommendation because published after it, and also because there is no evidence that this paper was used by the Commission in its IA. See: Paul R., Budnik L.T., Göen T., Hartwig A., MAK Commission (2017), Beryllium and its inorganic compounds – Determination of beryllium in urine by atomic absorption spectrometry, The MAK Collection for Occupational Health and Safety 2017, 2(4):1690-1709.

(RMM) needed to abide to the new OEL value. This is the reason why RPA has used three different methods to estimate the compliance costs for companies. However, rather than choosing just one of them, RPA states that 'the final cost-benefit conclusions take all the three methods into account, bearing in mind the advantages and disadvantages of each of them' (p. 88).

According to the IA, due to these compliance costs, if the strictest value were to be adopted without any transition period (i.e. option 2), a very limited number of companies might relocate (considering the higher OEL values in competitor countries) or close down. However, according to the IA, a transition period with a higher initial value (e.g. as in option 3 for Cd and option 4 for Be) would make it possible for them to implement changes gradually, and mitigate negative impacts on e.g. innovation (IA, p. 21). Considering the discussions in the context of the ACSH, the introduction of a transitional period, with less stringent values for cadmium and beryllium, is meant to address the concerns regarding the technical applicability and the costs of compliance deriving from an immediate application of the stricter selected values, and corresponds to the Commission's intention of finding a balanced approach between health considerations and economic impacts.[66]

This approach would also be consistent with Article 16 of the CMD which, while stating that scientific and technical data should be included in the basis on which OELs are set, specifies that '... binding OELs set under CMD must also reflect other factors such as 'feasibility' and take into account the views of the social partners' (IA, p. 162).[67]

Based on the comparison of policy options against the standard criteria of the Better Regulation Guidelines of effectiveness, efficiency, and coherence (IA, Table 7, p. 23 and Table 100, p. 27), the IA concludes by selecting as preferred options the values proposed by the ACSH, which only partially correspond to those proposed or recommended by SCOEL.

For cadmium and beryllium, the preferred values would be set after a transitional period of seven and five years, respectively, during which they will be fixed at the higher value indicated by Options 3 and 4, respectively. These two transitional period values were also recommended by the ACSH in their opinions, but not by SCOEL. In addition, a notation for respiratory and dermal sensitisation for beryllium would be included in Annex III to the CMD.

3.4.1. Evidence base

The Commission IA does not include a distinct reference list for each of the five carcinogens considered by the third amendment of the CMD. Rather, they are scattered throughout the report in correspondence of each carcinogen.

In the initial appraisal of the Commission IA, the author of this analysis stated that the IA could have been more transparent, for example on how data were gathered and from which sources to generate monetised information, and that the unavailability of the supporting study specifically commissioned from RPA prevented additional assessments. Having examined the reference listed in the RPA report, which is not published yet, and after examining the evidence base listed in the SCOEL and ACSH opinions and recommendations, it can be concluded that, overall, the impact assessment of the Commission has been based, directly and indirectly, on a vast amount of relevant and up-to-date information published in relevant scientific journals or by authoritative research centres and international organisations.

[66] The IA, in fact, states that it 'aims to balance health considerations against economic impacts, by proposing OELs that are still economically feasible while protecting a maximum number of workers' and that the proposal 'aims to take a balanced approach and to prevent industries from closures or severe disadvantages in particular Member States due to e.g. adopting the most stringent OELs' (IA, p. 20).

[67] The results of the social partners consultation are illustrated in Annex 2 of the IA (pp. 51-59).

It can also be added that the limitations and knowledge gaps regarding, for instance, the partial unavailability of epidemiological data, appear to be inherent to the analysis of the relationship between the exposure to a chemical substance and health endpoints. An example of a similar situation is provided in the Commission IA accompanying the proposal COM(2016) 350 final regarding the definition of criteria for identifying endocrine disruptors in the context of the implementation of the Plant Protection Products Regulation and Biocidal Products Regulation, SWD(2016) 211 final.

4. Selected methodological challenges

Based on the EMPL Committee's request, the following sections seek to provide additional explanations regarding some methodological challenges and knowledge gaps regarding in particular the disease burden and workers' exposure to Cd and Be, which have been acknowledged in the IA. The analysis provided does not claim to be exhaustive.

Before illustrating the analysis, it is worth mentioning what SCOEL states in the preamble regarding its 2017 methodology[68] for the derivation of OEL values of chemical agents. SCOEL, in fact, acknowledges that 'the derivation of OELs is a complex process. It is inevitably confronted with scientific uncertainty, especially with regard to health risks posed in the range of low exposure intensities. Moreover, the derivation of OELs is also dependent on the state of scientific knowledge at the time of obtaining the evidence, as well as the capabilities of detecting adverse health effects, such as subtle effects manifesting in humans over longer time-periods, e.g. neurodegenerative and autoimmune diseases. Consequently, SCOEL recognises that the proposed OELs need to be frequently reviewed as science progresses, new evidence becomes available and experience is gained' (p. 1)

4.1. Workers exposure to cadmium and beryllium

4.1.1. Workers exposure to cadmium

According to the RPA report on Cd (p. 33), the only identified multi-country estimate is the CAREX database, with further estimates being available for the Czech Republic, Finland, France, and the UK, as summarised in Table 10, while Table 11 refers to the data extrapolated to the EU-28.

Table 10: workforce exposed to cadmium and cadmium compounds - published data

Study	Country	Year/period	No. of exposed workers
Carex	EU-14	1990-1993 (mean)	207,000
	France	1990-1993	22,034
	Finland	1990-1993	1,040
	EU-5	1997	86,000
ICdA[43]	EU-28	2017	2,900
INRS[44]	France	2005	2,250-6,600
INRS (adjusted by ICdA)	France	2017	900-1,100
SUMER	France	2003	27,700
		2010	39,700
ASA[45]	Finland	2005	964
		2014	1,550
Regex	Czech Republic	2009-2016	49*
Note: *Cd only			

Source: RPA, Table 3-4 (p. 34), IA, Table 47 (p. 108)

[68] Scientific Committee on Occupational Exposure Limits (SCOEL), Methodology for derivation of occupational exposure limits of chemical agents. The general decision-making framework of the Scientific Committee on Occupational Exposure Limits, DG EMPL, Brussels, 6 December 2017.

Table 11: occupationally exposed population in the EU-28

Source estimate	EU-28 extrapolation
A: SUMER 2010 exposed workers in FR	300,000
B: CAREX EU14+5 mid-1990s	
D: ASA 2014 exposed workers in FI	140,000
E: ASA 2005 exposed workers in FI	90,000
F: INRS 2005 FR exposed workers in FR	17,000-50,000
G: INRS 2005 adjusted by ICdA for 2017, exposed workers in FR	6,800-8,400
H: ICdA 2017+consultation with individual companies	6,000-8,000
K: Regex 2009-16, exposed workers in CZ	2,400
Note: All extrapolations have been carried out on the basis of population. Extrapolation for estimate H also includes extrapolation on the basis of WEEE recycling statistics.	

Legend:
WEEE = waste electrical & electronic equipment
INRS = Institut national de recherche et de sécurité (France)
ICdA = international cadmium association

Source: RPA, Table 3-5 (p. 34)
IA, Table 48 (p. 109)

RPA states that using data from its occupational exposure biomonitoring programme, the ICdA estimates that approximately 2 900 workers are occupationally exposed to Cd in the EU. According to RPA, consultation with companies that are not ICdA members provides either direct evidence or indications that a further 3 000-5 000 workers might be exposed to Cd. This means that the total number of workers exposed to Cd, as indicated in the Table 11 above (H), would be between 6 000 and 8 000, although the possibility that all not relevant companies have responded to the consultation exercise would imply that the total exposed workforce could be greater (pp. 34-35).

With regard to the SUMER 2010 data (Table 11, A) which gives an extrapolated EU-28 number of workers exposed equal to 300 000, referring to data reported by the French medical monitoring survey of professional risks (surveillance médicale des expositions aux risques professionnels), RPA states that they are extrapolations from a sample of workers who self-declare exposure in a survey administered by company medical officers during the workers' compulsory medical examinations. For example, the data for 2003 reported in Table 16 above (27 700), were extrapolated from a sample of 84 workers which declared that they may have been exposed to cadmium and its compounds.

In addition to being data based on self-declarations, RPA states that they encompass a large number of workers that are exposed to low concentrations for short periods of time, pointing out that e.g. in the 2010 dataset, the majority of workers were exposed to 'very low' concentrations for less than 2 hours per week. Respondents were in fact considered exposed as soon as the agent was present at the workplace, regardless of the duration and intensity of exposure. As a result, according to RPA, 'workers in the SUMER dataset should be treated as 'potentially exposed' rather than exposed to specific concentrations, in particular since the exposure levels are extrapolated from a limited set of self-estimated values' (p. 37).

By contrast, according to RPA, the INRS (2005) and ICdA datasets provide lower estimates; although they were derived at different time, according to RPA they rely on comparable methods and the results are broadly consistent (p. 36).

In conclusion, according to RPA, the data collected through consultation provides evidence of around 6 000-8 000 workers currently exposed to Cd. 'However, only limited extrapolation from the responses received to some of the sectors has been possible and some indications of exposure could not be confirmed. In order to reduce the potential for this study to underestimate the exposed workforce, the core estimate taken forward for modelling is 10 000. This is complemented by an estimate of 30 000 considered within the framework of the sensitivity analysis' (p. 40).

The figure of 10 000 workers was taken forward by the Commission in its IA (IA, Table 1 'summary of estimates taken forward for the assessment of options', p. 5). However, the comment related to it included by the Commission in the table ('range of 2 900 - 300 000 between different estimates') should be considered in a different way in the light of the explanations provided by RPA.

According to the aforementioned explanations, the two values considered by RPA for its modelling, 10 000 and 30 000, appear to make sense, based on the availability of data at national and EU level, and the way some of them were gathered.

However, RPA acknowledges that a larger exposed workforce results in an increase to both the costs and benefits. Their extent, as well as the relative magnitudes of the cost and benefit increases, depends on the assumptions made about the concentrations to which the additional workers are exposed, and that 'the precise magnitude of the cost increases depends on the assumptions about the exposure concentrations that apply to these 20 000 additional workers. The additional modelling still supports the conclusion that the lowest reference OELV at which the monetised benefits may exceed the costs is 10 µg/m^3 (inhalable fraction), i.e. 4 µg/m^3 (respirable fraction)' (p. 131).

4.1.2. Workers exposure to beryllium

According to the RPA report on Be (pp. 51-62), three different methods were used to estimate the number of EU employees exposed to Be, all using 2015 data from the Occupational Safety and Health Administration (OSHA),[69] an agency of the United States Department of labor.

All three methods use its table IX-2 ('characteristics of industries affected by US-OSHA's proposed standard for beryllium'), providing the number of USA employees exposed to Be for each relevant NAIC [North American industry classification] code, which is mapped to the relevant NACE [nomenclature statistique des activités économiques dans la Communauté Européenne] code(s).

According to RPA, this data is available for seven of the sectors identified in the report, all except construction, laboratories and recycling. The three methods are referred to as BeST, EU/USA and US-OSHA.[70] The exposure concentrations were then applied to the employee and the enterprise data. After carrying out several calculations, not reported in this analysis, RPA concluded with an estimated number of workers affected by Be. These explanations, and the following tables, are also included in the annexes to the IA., namely:

[69] US-OSHA, Occupational Safety and Health Administration (2015), Occupational exposure to Beryllium and Beryllium compounds; proposed rule, available on: https://www.osha.gov/laws-regs/federalregister/2015-08-07

[70] **BeST**: according to BeST (beryllium science and technology association), the total number of employees exposed to beryllium in the EU is 12 000 to 13 000. The higher number was split across the seven sectors according to the proportions of exposed employees; the higher number was taken as this number is more likely to be an understatement rather than an overstatement;

EU/USA: the number of exposed employees in each of the seven sectors is multiplied by 1.5, which is the proportion of EU population (510 million) to USA population (326 million);

US-OSHA: the number of exposed employees in each of the seven sectors was divided by the total number of USA employees corresponding to the NACE code, giving the percentage of exposed employees in this industry. This number was then multiplied by the total number of EU employees for this NACE code.

Table 12: predicted employees affected by beryllium by sector

Sector	Predicted number of EU employees exposed to beryllium (BeST)	Predicted number of EU employees exposed to beryllium (EU/USA)	Predicted number of EU employees exposed to beryllium (US-OSHA)	CAREX estimate of EU employees exposed to beryllium
Foundries	1,276	5,099	10,205	2,620
Metal fabrication	4,878	19,491	27,225	5,743
Transportation	801	3,202	4,149	4,394
ICT	408	1,628	1,386	3,798
Specialist manufacturers	2,272	9,079	15,193	46,265
Medical devices	3,188	12,737	11,323	1,040
Glass	177	709	783	2,129
Laboratories	410*	1,639*	2,556*	N/A
Recycling	122*	487*	760*	N/A
Total excluding construction	**13,532**	**54,071**	**73,580**	**65,989**
Construction	6,624*	26,469*	41,276*	490
Total	**20,156**	**80,540**	**114,856**	**66,479**
Source: Modelling by RPA, Carex (undated), US-OSHA (2015), BeST *Note: *Based on estimated percentages of employees affected by beryllium, see Table 3.14*				

Source: RPA, Table 3-19 (p. 57); IA, Table 55 (p. 124)

According to RPA, the figures using the BeST data 'appear to be too low: it seems likely that BeST has included the companies that it supplies and their employees, but has not allowed for the companies that are further down the supply chain' (p. 57). A comparison of the estimates of workers exposed to Be is shown in the following table:

Table 13: occupationally exposed population in the EU-28

Source estimate	EU-28 extrapolation
CAREX EU14+5 mid-1990s & IOM (2011)	65,000
ASA 2014 exposed workers in Finland	12,500
BeST	12,000 – 13,000
RPA - BeST	13,532, (20,156)
RPA – EU/US	54,071, (80,540)
RPA – US-OSHA	73,580, (114,856)
Source: Modelling by RPA, CAREX (undated), ASA Finland (2014), IOM (2011), BeST (unpublished) *RPA values exclude construction; values including construction are in brackets.* *Note: ASA Finland extrapolation is based on population.*	

Source: RPA, Table 3-20 (p. 58)[71]

According to RPA, CAREX EU and the IOM (Institute of occupational medicine) predicted approximately 65 000 workers exposed in the EU, but many stakeholders, not only BeST, consider this to be too high. The estimate using the EU/USA method arrives at a figure of 54 071 excluding construction, higher than the 13 000 of BeST and lower than the CAREX/IOM figure. Examining the data from the USA, and the number of workers in the EU in each of the sectors, RPA concludes that

[71] This table is not provided in the Commission IA, as in other few cases of tables included in this analysis. As such, the RPA source will not include the corresponding cross-reference to the Commission IA.

'the EU/USA figures are the most plausible' (p. 58). As such, the EU/USA figures were used in the RPA analysis; this figure is the value chosen by the Commission in its IA (see the Table 13 above).

However, RPA states that 'the greatest uncertainty is exposure distribution. If parts of the EU do have higher exposure levels than the BeST survey implies and closer to the USA distribution, then the costs, and hence company closures, would be significantly higher at all target OELVs: benefits are also significantly higher' (p. 154).

4.2. Disease burden

The analysis of the economic impact of ill-health, which can be considered distinct but complementary to the clinical or epidemiological approaches to disease burden, has been mainly carried out by using some variant of the Cost-of-Illness (COI) methodology, first formalised in the mid-1960s,[72] though macroeconomic growth models have increasingly been used to better understand the dynamic and multifaceted nature of losses at the societal level.[73]

The aim of COI studies is to assess the economic burden that a specific health problem (or groups of health conditions) imposes on a society, usually with respect to the utilisation of health care resources and productivity losses. This is done by identifying and measuring all the costs of a disease, including the direct, indirect, and intangible dimensions, and expressing the output in monetary terms.

Direct costs are those incurred by the health system, society, family and individual patient; they consist of healthcare and non-healthcare costs. The former includes hospitalisation services, physician and nurse services, long-term care, prescription drugs, medical supplies and laboratory tests. The latter are related to the consumption of non-healthcare resources like transportation, household expenditures, relocating, property losses, and informal cares of any kinds.[74]

Indirect costs, in COI studies, occasionally refer to productivity losses due to morbidity and mortality, borne by the individual, family, society, or the employer. They are estimated through different methods, one of these being the Willingness-to-pay method (WTP) used by RPA. WTP measures, through various methods (e.g. surveys, examining the extra wages for highly risky jobs, examining the demand for products that leads to greater level of health or safety), the amount that an individual is eager to pay in order to reduce the probability of illness or mortality.[75] On the European chemicals agency (ECHA) website WTP values are available for health outcomes in relation to chemicals.

Intangible costs capture the psychological dimensions of the illness to the individual (and their family), i.e. the pain, anxiety and suffering; these costs are not usually monetised, because objective valuations of these impacts are rarely available or easily validated, due to the measurement difficulties and related controversies.[76] These costs have therefore been expressed as non-monetary

---

[72] Rice D.P. (1967), Estimating the Cost of Illness. Estimating the cost of illness. American Journal of Public Health 57(3):424–40.

[73] WHO (2009), WHO guide to identifying the economic consequences of disease and injury, Geneva (App. C).

[74] On the economic valuation of informal care see, for instance, Van Den Berg B., Brouwer W.B.F, Koopmanschap M.A. (2004), Economic valuation of informal care: an overview of methods and applications. The European Journal of Health Economics 5(1):36-45.

[75] Attempts to implement this approach using survey responses or revealed preferences estimates have produced values affected by statistical problems and measurement difficulties. On this issue see, for instance, Landefeld J.S., Seskin E.P. (1982), The economic value of life: linking theory to practice. American Journal of Public Health 72(6):555-66.

[76] Cooper B.S., Rice D.P. (1976), The economic cost of illness revisited. Social Security Bulletin 39(2):21-36. They conclude that estimates based on the human capital approach, reformulated using a willingness-to-pay criterion, produce the only clear, consistent, and objective values.

measures, such as DALYs (Disability Adjusted Life Years) or QALYs (Quality Adjusted Life Years); these are measures that combine and standardise health care costs and the 'lost economic or societal contribution' resulting from premature death or disability.[77]

The approach used by the Commission for the monetisation of ill health effects is explained in Annex 4 of the IA (pp. 66-79), which takes into account two approaches to the monetisation of intangible costs (IA, p. 74).

4.2.1. Disease burden estimated by RPA: cadmium

RPA, in its report on Cd, considers two health endpoints to calculate the current (CDB) and future (FDB) burden of disease and the (changes in the) costs caused by ill health associated to Cd exposure: lung cancer and elevated proteinuria. RPA states that other relevant endpoints which have not been quantified include kidney and prostate cancer, and osteotoxic (toxic to the bones) or respiratory effects (p. 70).

CDB and FDB, expressed as number of cases of lung cancer[78] and increased proteinuria[79] over 40 and 60 years, have been estimated assuming that the numbers of workers in the relevant sectors and the exposure concentrations have been decreasing by a combined 7% per annum (p. 64).

With regard to the CDB, RPA states that its estimates only relate to the sectors where exposure to Cd currently occurs and do not represent the total burden of past occupational exposure to Cd. This is because 'the total burden from all past occupational exposure to Cd would require consideration of sectors where occupational exposure no longer takes place and which may not be relevant to the problem definition for this Impact Assessment' (p. 65).[80]

With regard to the FDB, RPA states that the number of cases of lung cancer and proteinuria expected to occur in the future is illustrated in the following tables for a workforce of 10 000 workers. The estimates are based on the assumption that the number of workers exposed to Cd, and the associated exposure concentrations, will remain unchanged over time.

However, two sets of estimates are provided: one assumes a constant exposed workforce, while the second set takes into account staff turnover, i.e. the fact that some percentage of staff might change occupation or leave work and be replaced in any given year. A 5 % turnover is assumed by RPA for its estimates.

The number of cases of lung cancer and proteinuria estimated by RPA are the following:

---

[77] DALY measures the loss of one year of healthy life, therefore illustrating the negative impact of a condition, and they are commonly used to quantify the burden of disease at a population level. QALYs are used to illustrate health benefits: they are life years adjusted by a quality weight, which is measured on a preference scale, where 'full health' equals a score of 1.0, being 'dead' a score of 0.0.

[78] With regard to lung cancer, RPA states that the exposure-risk relationship (ERR) is applied on an estimated workforce/concentrations halfway through a past assessment period of 40 years which is assumed to have expired 30 years ago (30 years is expected to be the average latency for lung cancer). The CBD is thus approximated based on the estimated number of workers and exposure concentrations 50 years ago (1/2 of risk over 40 years and a latency period of 30 years) (p. 64).

[79] Regarding elevated proteinuria, the CBD is approximated with reference to the workforce and concentrations 20 years ago (halfway through the period to which the DRR applies). (p. 64).

[80] RPA also points out that recent regulatory developments, such as REACH Annex XVII entry 23 general restriction, have resulted in a significant reduction in terms of the workforce exposed to Cd and the associated exposure concentrations. According to RPA, this means that although the burden of historical exposure to Cd may be relatively significant due to the large number of sectors where exposure occurred in the past and the long latency periods, the scope for further health benefits due to an OEL value is limited to the sectors/uses where occupational exposure to Cd still occurs: these have been the focus of the RPA study (p. 65).

Table 14: current burden of disease due to past exposure to cadmium

Endpoint	Cases per annum
Lung cancer	11 new registrations each year
Increased proteinuria	Around 500 people living with increased proteinurea
Source: modelling by the study team	

Source: RPA, Table 3-26 (p. 65)

Table 15: future burden of disease (baseline) for a constant workforce of 10 000 workers

Endpoint	Number of cases over 40 years	Number of cases over 60 years	Monetary value PV 60 years[66]	
			Static discount rate	Declining discount rate
Lung cancer	3.4	5.8	€5 million	€5 million
Increased proteinuria	95	181	€9-42 million	€9-43 million

Legend: PV = present value 66 = Static discount rate: 4% per year; declining discount rate: 4% per year for the first 20 years, 3% per year thereafter.

Source: RPA, Table 3-27 (p. 65)

Table 16: future burden of disease (baseline) for a workforce of 10 000 workers and turnover

Endpoint	Number of cases over 40 years	Number of cases over 60 years	Monetary value PV 60 years[67]	
			Static discount rate	Declining discount rate
Lung cancer	3.4	5.8	Same as 'no turnover' scenario	
Increased proteinuria	190	280	€13-61 million	€13-63 million

Legend: PV = present value 67 = Static discount rate: 4% per year; declining discount rate: 4% per year for the first 20 years, 3% per year thereafter.

Source: RPA, Table 3-28 (p. 65)

4.2.2. Disease burden considered by the Commission: cadmium

The Commission, in its IA (Table 5, pp. 20-21) presents a table regarding the CDB and FDB and the corresponding monetary values for lung cancer and other adverse effects, which correspond to the increased proteinuria calculated by RPA. In fact, the IA states that only two health endpoints have been quantified, lung cancer, and proteinuria while kidney and prostatic cancer, osteotoxic and respiratory effects have not been quantified.

The resulting table presents the baseline scenario identified by the Commission:

Table 17: baseline scenario over 60 years for cadmium and its inorganic compounds

Other adverse health effects	[increased] Proteinurea
Number of exposed workers	10 000
Change exposure level	Past: -7 % p.a. (level and workers) Future: 0 %
Change no. of exposed workers	Past: -7 % p.a. (level and workers) Future: 0 %
Current disease burden (CDB) - no. of cancer cases	11
Future disease burden (FDB) - no. of cancer cases	5.8
CDB no. of other adverse health effects [increased proteinuria]	500
FDB no. of other adverse health effects [increased proteinuria]	180-280 *
Exp. no. of deaths FDB cancer	5

Exp. no. of deaths FDB other adverse health effects [increased proteinuria]	6-8
Monetary value FDB cancer	EUR 5 million
Monetary value FDB other adverse health effects [increased proteinuria]	EUR 9-63 million
Legend: * = workforce turnover at 5 % per annum	Source: IA, Table 5 (p. 20), based on RPA, Tables 3-26/27/28/29 (p. 65-66)

Comparing the IA table 17 with the RPA tables 14-16, and with the RPA Tables 3-29, not included in this analysis (summarising the baseline scenario), it seems useful to point out what follows:

- FDB – no. of cancer cases: the indicated value of 5.8 has been obtained by multiplying the number of additional yearly cases (0.1) over 60 years;
- FDB – no. of other adverse health effects [increased proteinuria]: the indicated value of 180-280 should include the CDB, represented by 500 people already leaving with elevated proteinuria (see Table 5);
- Exp. no. of deaths FDB cancer: the indicated value of 5 should also include the CDB;
- Exp. no. of deaths FDB other adverse health effects [increased proteinuria]: the indicated value of 6-8 should also include the CDB;
- Monetary value FDB cancer: the indicated value of EUR 5 million should also include the monetary value of the CDB for cancer;
- Monetary value FDB other adverse health effects [increased proteinuria]: the indicated value of EUR 9-63 million should also include the monetary value of the CDB for increased proteinuria.

RPA states that the assessment it has carried out for Cd, as summarised in Tables 14-16, does not capture the full CDB and FDB from historic exposures to Cd for the following reasons (pp. 66-67):

- not all past uses of Cd are covered in the assessment as only current uses, and therefore current exposures, are considered;
- the assessment of the disease burden does not factor in the existence or not of OEL values over the past 40 years. In addition, it does not consider changes in national OEL values over time;
- not all health endpoints could be quantified and monetised.

According to RPA, the implications of these factors is that the current burden of disease may be underestimated. As table 17 is based on the calculations performed by RPA, the aforementioned comments made by RPA can be applied identically to the values indicated in the corresponding Table 5 of the Commission IA (p. 20).

4.2.3. Disease burden estimated by RPA: beryllium

RPA, in its report on Be, considers two health endpoints to calculate the CDB and FDB and the (changes in the) costs caused by ill health associated to Be exposure: cancer and chronic beryllium disease (CBD). RPA states that other relevant endpoints which have not been quantified include Be sensitisation (BeS).

RPA acknowledges that there may be other non-cancer endpoints such as adverse local respiratory effects, secondary haematological effects and skin sensitisations as a result of dermal contact. However, according to RPA, should they occur, they are likely to happen at higher occupational exposures; in any case, a quantitative sensitivity analysis of these effects is not feasible, for the reasons which are illustrated in the report (p. 143).

Similarly, to what has been done for Cd, RPA states that Be estimates only relate to the sectors where exposure to Be currently occurs and do not represent the total burden of past occupational exposures to it. According to RPA, in fact, calculating the total burden from all past occupational exposure to Be would require consideration of sectors where occupational exposure no longer takes place and which are not relevant to the problem definition for this study (p. 79).

RPA states that the CDB is estimated using data regarding all sectors excluding construction, based on the EU/US data for exposed employees and the BeST distribution. The CDB is considered as the number of cases (i.e. workers) currently suffering from CBD based upon the last 40 years' exposure and assumes that the numbers of workers in the relevant sectors have decreased by 1 % per year and that exposure concentrations have decreased by 3 % per year (pp. 78-79).

Table 18: current burden of disease (CBD) due to past exposure to Be

Endpoint	Number of cases currently suffering from CBD
Seven sectors (US-OSHA distribution)	5,564
Seven sectors (BeST distribution)	3,657
Nine sectors (BeST distribution)	3,807
Ten sectors (BeST distribution)	5,670
Source: Modelling by RPA *Dataset - EU/US; Exposure distribution - BeST and US-OSHA; Sectors – seven (excluding construction, laboratories and recycling), nine (excluding construction) and ten (all sectors)*	

Source: RPA, Table 3-33 (p. 79)

As regards the BeST distribution, RPA states that 'BeST say that the total number of employees exposed to beryllium in the EU is 12 000 to 13 000. The higher number, 13 000, was split across the seven sectors [seven sectors estimated with the BesT distribution, see Table 18] or according to the proportions of exposed employees. The higher number was taken as this number is more likely to be an understatement rather than an overstatement' (p. 52).

As regards the US-OSHA distribution, RPA states that 'the number of exposed employees in each of the seven sectors is multiplied by 1.5, which is the proportion of EU population (510 million) to US population (326 million)' (p. 52). Two scenarios are modelled by RPA for the exposed workforce (p. 85):

- constant workforce: the workforce remains unchanged over 40 years (same worker, no replacement of workers affected by ill health), and in year 41 the whole workforce is replaced, with these workers remaining in the exposed workforce over the next 40 years. According to RPA, this scenario does not take into account either the natural turnover of workers changing jobs or the turnover due to the ill health caused by exposure to the relevant chemical agents:
- workforce turnover of 5 % per year: there is a turnover of 5 % per year, implying that the whole workforce is replaced every 20 years and no worker is exposed for the full 40 year period (modelled by RPA as a group of workers being exposed for a 20 year period, followed by another group of workers exposed over the subsequent 20 years). According to RPA, this scenario increases the number of cases for non-cancer endpoints. The turnover caused by treatment or early retirement due to the conditions considered has not been modelled.

The following tables provide the number of cancer and CBD cases over 40 and 60 years estimated for the two aforementioned scenarios:

Table 19: future burden of disease (CBD, baseline) - constant workforce

Endpoint	Number of cases over 40 years	Number of cases over 60 years	Monetary value PV 60 years Method 1 – Method 2	
			Static discount rate (4%)	Declining discount rate (4% for 20 years, then 3%)
Seven sectors (US-OSHA distribution)	2,279	4,558	€430 million – €1.7 billion	€480 million – €1.8 billion
Seven sectors (BeST distribution)	1,473	2,946	€280 million – €1.1 billion	€310 million – €1.2 billion
Nine sectors (BeST distribution)	1,534	3,068	€290 million – €1.2 billion	€320 million – €1.2 billion
Ten sectors (BeST distribution)	2,284	4,568	€440 million – €1.7 billion	€480 million – €1.8 billion
Source: Modelling by RPA *Dataset - EU/US; Exposure distribution - BeST and US-OSHA; Sectors – seven (excluding construction, laboratories and recycling), nine (excluding construction) and ten (all sectors)* *All financial values are relative to the baseline.*				

Legend: PV = present value of the direct, indirect, and intangible costs of each case Source: RPA, Table 3-34 (p. 79)

As regards the number of cases of cancer, RPA states that no avoided cases of cancer are predicted for the proposed OEL values as the levels required to cause it (>10 µg/m^3) are well above those at which companies across the EU are currently operating (p. 82), and that most EU companies using Be are already operating at exposure levels within the target range of the OEL values, i.e. below 2 µg/m^3 (p. 83).

4.2.4. Disease burden considered by the Commission

The IA of the Commission contains a Table (Table 8, p. 24) presenting the CDB and FDB and the monetary values corresponding to the FDB for one endpoint, CBD. The IA states, in fact, that allergy or asthma symptoms, beryllium respiratory sensitisation, skin sensitisation, cardiovascular, renal, hepatic and haematological effects have not been quantified. The resulting table presents the baseline scenario identified by the Commission:

Table 20: baseline scenario over 60 years for beryllium

No. of exp. workers	54 071 (excluding construction sector) *
Change in exposure levels	Past: -3 % per year Future: Expected 2 % per year reduction
Change number of exposed workers	Past: -1 % per year Future: Expected 3 % per year reduction
Current disease burden (CDB) no. of cancer cases	*None*
Future disease burden (FDB) no. of cancer cases	*None*
Current disease burden (CDB) - no. of chronic beryllium disease cases	Exposure in sectors considered [by RPA] over the past 40 years: 3 807
Future disease burden (FDB) - no. of chronic beryllium disease cases	3 068-4 602 ** *Constant workforce* 3 068 *over 60 years (51 per year) Workforce turns over at 5% per year* 4 602 *over 60 years (77 per year)*
Exp. no. of deaths (FDB) from chronic beryllium disease	307-460 **

	Constant workforce 307 *over 60 years (5 per year)* *Workforce turns over at 5% per year 460 over 60 years (8 per year)*
Monetary value FDB from adverse health effects	EUR 290 million – EUR 1.9 billion *Constant workforce - EUR 290 million (Method 1), EUR 1.2 billion (Method 2)* *Workforce turns over at 5% per year - EUR 420 million (Method 1), EUR 1.9 billion (Method 2)*
Legend: in italics, information included in the original RPA Table * = this estimate has been chosen by RPA as the most plausible after examining data from the USA, and the number of workers in the EU in each of the sectors where workers are exposed to Be (RPA, p. 58). ** = workforce turnover at 5% per annum	Source: IA, Table 8 (p. 24), based on RPA, Tables 3-33/34/35/36/37/38 (pp. 79-82)

The IA acknowledges that the assessment does not capture the full burden of CBD and cancer (current and future) from historic exposures to Be for the following reasons:

- not all past uses of Be are covered, as only current uses, and therefore current exposures, are considered;
- the assessment of the disease burden does not factor in the existence or not of OEL values over the past 40 years. In addition, it does not consider changes in national OEL values over time.

According to RPA, the implications of these two factors are that the CDB related to cancer cases may be underestimated, as may the burden of disease related to CBD. As Table 20 is based on the calculations performed by RPA, the aforementioned comments made by RPA can be applied identically to the values indicated in the corresponding Table 8 of the Commission IA.

Conclusions

Based on this detailed appraisal of the impact assessment (IA) accompanying the Commission proposal for a third amendment of the Carcinogens and Mutagens Directive 2004/37/EC (CMD), which focuses on the process and evidence base used in the IA for setting the limit values for cadmium and beryllium, the following conclusions can be drawn.

The Commission has based the selection of its preferred options on the same process as the one adopted for the first and second amendment of the CMD.

Firstly, the Scientific Committee on Occupational Exposure Limits (SCOEL), has proposed or recommended a set of occupational exposure level (OEL), short-term exposure level (STEL), and biological guidance level (BGL) values, in addition to a notation for dermal and skin sensitisation for beryllium. These recommendations and opinions, according to the Commission decision setting up the SCOEL, have to be based on the latest scientific evidence on the health effects of chemical agents on workers at work.

Secondly, the Advisory Committee on Safety and Health at Work (ACSH), a tripartite body set up in 2003 to streamline the consultation process in the field of occupational safety and health, has issued opinions on them, also taking into considerations the opinions of the three interest groups represented within it (employers, workers, and government).

Thirdly, the external contractors (RPA, FoBiG, COWI, and EPRD Office for Economic Policy and Regional Development) engaged by the Commission, have carried out a cost-benefit and a multi-criteria analysis to analyse the health, socio-economic and environmental impacts deriving from the introduction of a range of OEL values. Their analysis has been performed considering a set of OEL reference values, which included also the values recommended/proposed by SCOEL and the ACSH.

Finally, after considering the main findings obtained by the external contractors, which are extensively reported in the IA, the Commission has carried out a comparison of the options retained for further assessment, based on the Better Regulation Guidelines' criteria of efficiency, effectiveness, and coherence. This study concludes that the Commission selected as preferred option for cadmium the strictest OEL value recommended by SCOEL, endorsed by the ACSH (IA option 2), with a transitional OEL value proposed by the ACSH, but not recommended by SCOEL. However, for beryllium, the Commission decided to select as preferred option the OEL value proposed by the ACSH (IA option 3), while the SCOEL recommended an OEL value 10 times stricter. In addition, the Commission decided to endorse the ACSH proposal for a transitional higher OEL value (i.e. less stringent), which the SCOEL did not recommend. The Commission's decision regarding beryllium appears to be supported by the analysis carried out by the external contractors.

In particular, for cadmium, the preferred OEL value of 1 µg/m^3 (inhalable dust fraction) would be set after a transitional period of seven years, during which it would be fixed at the higher value of 4 µg/m^3 (inhalable dust fraction). The IA does not appear to have taken up the ACSH's request to investigate whether a combined biomonitoring and time-weighted OEL approach could be included in the CMD.

For beryllium, the preferred OEL value of 0.2 µg/m^3 (inhalable dust fraction) would be set after a transitional period of five years, during which a higher value of 0.6 µg/m^3 (inhalable dust fraction) would be fixed. In addition, a notation for dermal and respiratory sensitisation would be added to annex III of the CMD. As before, the IA does not appear to have taken up the ACSH's proposal to set a biomonitoring guidance value of 0.04 µg/l urine, which was also recommended by SCOEL. However, referring to the options proposing to include a biological monitoring or binding biological limit values, the IA states, without providing further information, that it is currently legally not possible to establish such limit values under the CMD.

Considering the discussions in the context of the ACSH, the introduction of a transitional period, with less stringent values for cadmium and beryllium, is meant to address the concerns regarding the technical applicability and the costs of compliance deriving from an immediate application of the stricter selected values, and corresponds to the Commission's intention of finding a balanced approach between health considerations and economic impacts.

As regards the evidence base used in the IA for setting the preferred OEL values, the IA has relied on a vast amount of up-to-date information, including scientific journals, guidelines, manuals and surveys, published by authoritative research centres, publishers and international organisations, making the overall analysis convincing and robust.

Concerning the limitations of the assessment, which are transparently acknowledged, the analysis carried out by the external contractors and endorsed in the IA recognises that the full current and future disease burden deriving from historic exposures to cadmium and beryllium is not captured.

Consequently, the disease burdens may be underestimated, for at least the following reasons:

- not all past uses of cadmium are covered as only current uses, and therefore current exposures, are considered;
- the assessment of the disease burden does not factor in the existence, or otherwise, of OEL values over the past 40 years. In addition, it does not consider changes in national OEL values over time;
- only two health endpoints for cadmium (lung cancer, and proteinuria) and two for beryllium (cancer and chronic beryllium disease) could be quantified and monetised, while kidney and prostatic cancer, and osteotoxic and respiratory effects have not been quantified for cadmium, and nor has beryllium sensitisation for beryllium.

As regards the estimated number of workers exposed to cadmium, the value of 10 000 workers considered by the external contractors for their modelling (in addition to a higher value of 30 000), and taken over in the IA, is coherently justified in light of the recognised wide divergences among the different estimates. This value appears to be reasonable, based on the availability of data at national and EU level, and the way some of them were gathered.

As regards the estimated number of workers exposed to beryllium, the figure of 54 071 workers exposed in the EU 28 (excluding the construction sector) identified by the external contractor and used in the IA appears to be plausible, based on the justifications provided. However, it is acknowledged that exposure to higher (i.e. less stringent) limit values would imply higher costs and benefits at all target OEL values.

References

Adams S.V. and Newcomb P.A. (2014), Cadmium blood and urine concentrations as measures of exposure: NHANES 1999–2010. Journal of exposure science and environmental epidemiology 24(2):163-170.

Advisory Committee on Safety and Health at Work (ACSH), working party on chemicals. Mandate 2017-2020, Doc. 1818/16, ACSH, Brussels, 30 November 2016.

Advisory Committee on Safety and Health at Work (ACSH) – Minutes of the working party on chemicals at the workplace, Doc. 343-18, DG EMPL, Luxembourg 21-22nd March 2017.

Advisory Committee on Safety and Health at Work (ACSH), Opinion on an EU occupational exposure limit value for beryllium and inorganic beryllium compounds under Directive 2004/37/EC (CMD), Doc. 662/17, ACSH, Brussels, 31 May 2017.

Advisory Committee on Safety and Health at Work (ACSH), Opinion on an EU occupational exposure limit value for cadmium and its inorganic compounds under Directive 2004/37/EC (CMD), Doc. 663/17, ACSH, Brussels, 31 May 2017.

BAuA (Bundesanstalt für Arbeitsschutz und Arbeitsmedizin), Begründung zu ERB Cadmium in TRGS 910 [Technische Regel für Gefahrstoffe], Annex 3, BAuA, Dortmund/Berlin, 2014.

Beryllium science & technology association (BeST), Comments for consideration by the SCOEL. Borak J. (2016), CIRCABC website, 31 May 2016.

Chaumont A., Voisin C., Deumer G., Haufroid V., Annesi-Maesano I., Roels H., et al. (2013), Associations of urinary cadmium with age and urinary proteins: further evidence of physiological variations unrelated to metal accumulation and toxicity. Environmental Health Perspectives 121(9):1047–1053.

Chaumont A. and Bernard A.C. (2013), Urinary cadmium as a marker of exposure in epidemiological studies: Bernard and Chaumont respond. Environmental Health Perspectives 121(10):A296–A297.

Cooper B.S., Rice D.P. (1976), The economic cost of illness revisited. Social Security Bulletin 39(2):21-36.

Council of the European Union, Decision setting up an Advisory Committee on Safety and Health at Work, 2003/C218/01, Brussels, 22 July 2003.

Council of the European Union, Employment, Social Policy, Health and Consumer Affairs (EPSCO), Council conclusions on a new agenda for health and safety at work to foster better working conditions, Brussels, 5 October 2015.

European Commission, Decision on setting up a Scientific Committee on Occupational Exposure Limits for Chemical Agents and repealing Decision 95/320/EC, Decision 2014/113/EU, Brussels, 3 March 2014.

European Commission, Request for a recommendation on occupational exposure limit value(s) ('OELs) and/or a scientific opinion in accordance with Commission Decision 2014/113/EU: Beryllium and inorganic Beryllium compounds, DG EMPL, Luxembourg, 14 December 2014.

European Commission, Decision appointing members of the Scientific Committee on Occupational Exposure Limits for Chemical Agents for a new term of office, C(2015) 2369 final, Brussels 14 April 2015.

European Commission, proposal for a directive of the European Parliament and of the Council amending Directive 2004/37/EC on the protection of workers from the risks related to exposure to carcinogens or mutagens at work, COM/2016/0248 final, Brussels, 13 May 2016.

European Commission, Request for a recommendation on occupational exposure limit value(s) ('OELs) and/or a scientific opinion in accordance with Commission Decision 2014/113/EU: Cadmium and inorganic compounds, DG EMPL, Luxembourg, 12 December 2016.

European Commission, proposal for a directive of the European Parliament and of the Council amending Directive 2004/37/EC on the protection of workers from the risks related to exposure to carcinogens or mutagens at work, COM/2017/011 final, Brussels, 10 January 2017.

European Commission, Communication on a safer and healthier work for all – Modernisation of the EU occupational safety and health legislation and Policy, COM/2017/012 final, Brussels, 10 January 2017.

European Commission, Better Regulation Guidelines, Commission staff working document SWD (2017) 350, Brussels, 7 July 2017.

European Commission, Third study on collecting most recent information for a certain number of substances with the view to analyse the health, socio-economic and environmental impacts in connection with possible amendments of Directive 2004/37/EC on the protection of workers from the risks related to exposure to carcinogens or mutagens at work (VC/2017/0011), DG EMPL, Luxembourg, 7 August 2017.

European Commission, proposal for a directive of the European Parliament and of the Council amending Directive 2004/37/EC on the protection of workers from the risks related to exposure to carcinogens or mutagens at work, COM/2018/0171 final, Brussels, 5 April 2018.

European Commission, Impact assessment accompanying the proposal for a Directive of the European Parliament and of the Council amending Directive 2004/37 on the protection of workers from the risk related to exposure to carcinogens or mutagens at work, Commission staff working document SWD/2018/088 final, Brussels, 5 April 2018.

European Parliament and Council of the European Union, Directive 2004/37/EC of the European Parliament and of the Council of 29 April 2004 on the protection of workers from the risks related to exposure to carcinogens or mutagens at work (sixth individual directive within the meaning of Article 16(1) of Council Directive 89/391/EEC, Brussels, 29 April 2004.

European Parliament, Resolution of 25 November 2015 on the EU Strategic Framework on Health and Safety at Work 2014-2020 (2015/2107(INI)).

Georgescu A.A., Protection of workers from exposure to carcinogens or mutagens, initial appraisal of a Commission IA, EPRS, European Parliament, 18 July 2016.

Kidney Disease Improving Global Outcomes (2013), KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney International 3(2):1-150.

Landefeld J.S., Seskin E.P. (1982), The economic value of life: linking theory to practice. American Journal of Public Health 72(6):555-66.

Rice D.P. (1967), Estimating the Cost of Illness. American Journal of Public Health 57(3):424–40.

Risk & Policy Analysts (RPA), Forschungs- und Beratungsinstitut Gefahrstoffe (FoBiG), COWI, and EPRD Biuro Polityki Gospodarczej i Rozwoju Regionalnego, Third study on collecting most recent information for a certain number of substances with the view to analyse the health, socio-economic and environmental impacts in connection with possible amendments of Directive 2004/37/EC - Cadmium and its inorganic compounds, Final report, prepared for the European Commission, DG EMPL, Brussels, 8 February 2018 (**report not yet published**).

RPA et al., Third study on collecting most recent information for a certain number of substances with the view to analyse the health, socio-economic and environmental impacts in connection with possible amendments of Directive 2004/37/EC - Beryllium, Final report prepared for the European Commission, DG EMPL, Brussels, 8 February 2018 (**report not yet published**).

RPA et al., Third study on collecting most recent information for a certain number of substances with the view to analyse the health, socio-economic and environmental impacts in connection with possible amendments of Directive 2004/37/EC - OEL/STEL deriving systems, Final report prepared for the European Commission, DG EMPL, Brussels, 8 February 2018 (**report not yet published**).

RPA et al., Third study on collecting most recent information for a certain number of substances with the view to analyse the health, socio-economic and environmental impacts in connection with possible amendments of Directive 2004/37/EC - Methodological note, Final report prepared for the European Commission, DG EMPL, Brussels, 8 February 2018 (**report not yet published**).

Scholz N., Limits on exposure to carcinogens and mutagens at work: second proposal, EPRS, European Parliament, 29 May 2017.

Scholz N., Limits on exposure to carcinogens and mutagens at work, EPRS, European Parliament, 22 January 2018.

Scholz N., Limits on exposure to carcinogens and mutagens at work: third proposal, EPRS, European Parliament, 2 October 2018.

Scientific Committee on Occupational Exposure Limits (SCOEL), Recommendation from the Scientific Committee on Occupational Exposure Limits for cadmium and its inorganic compounds, SCOEL/SUM/136, Brussels, February 2010.

Scientific Committee on Occupational Exposure Limits (SCOEL), Opinion from the Scientific Committee on Occupational Exposure Limits for Cadmium and its inorganic compounds, SCOEL/OPIN/336, Brussels, 8 February 2017.

Scientific Committee on Occupational Exposure Limits (SCOEL), Opinion from the Scientific Committee on Occupational Exposure Limits for Beryllium and inorganic Beryllium compounds, SCOEL/REC/175, Brussels, 8 February 2017.

Scientific Committee on Occupational Exposure Limits (SCOEL), Draft agenda of the plenary meeting, SCOEL-100, DG EMPL, Berlin, 8-10 February 2017.

Scientific Committee on Occupational Exposure Limits (SCOEL), Methodology for derivation of occupational exposure limits of chemical agents. The general decision-making framework of the Scientific Committee on Occupational Exposure Limits, DG EMPL, Brussels, 6 December 2017.

Scott M.A., Angerer J., Boogaard P.J., Hughes M.F., O'Lone R.B., Robison S.H, Schnatter A.R., (2013), The use of biomonitoring data in exposure and human health risk assessment: benzene case study. Critical Review in Toxicology 43(2):119–153 (pp. 120-121).

Strupp C. (2011), Beryllium metal II. A review of the available toxicity data. The Annals of Occupational Hygiene 55(1): 43–56.

Van Den Berg B., Brouwer W.B.F, Koopmanschap M.A. (2004), Economic valuation of informal care: an overview of methods and applications. The European Journal of Health Economics 5(1):36-45.

Vettorazzi S., Protection of workers from exposure to carcinogens or mutagens: second proposal, initial appraisal of a Commission IA, EPRS, European Parliament, 13 July 2017.

Vettorazzi S., Protection of workers from exposure to carcinogens or mutagens: third proposal, initial appraisal of a Commission IA, EPRS, European Parliament, 27 June 2018.

World Health Organization (WHO), WHO guide to identifying the economic consequences of disease and injury. WHO, Geneva (App. C), 2009.

QA-06-18-276-EN-N

The European Commission proposal COM(2018) 171 final seeks to amend the Carcinogens and Mutagens Directive 2004/37/EC by establishing binding occupational exposure limit (OEL) values for five carcinogenic chemical agents.

Following an initial appraisal by EPRS of the strengths and weaknesses of the European Commission's impact assessment (IA) accompanying the proposal, the European Parliament's Committee on Employment and Social Affairs requested a more detailed and focused appraisal regarding the process and evidence base used in the IA for setting the limit values for cadmium and beryllium, as well as some of the limitations of the analysis performed in the IA.

This study illustrates how an initial set of values were identified, selected for further assessment and subsequently chosen by the Commission.

As regards the evidence base used in the IA for setting the preferred OEL values, the study shows that the IA has relied on a vast amount of up-to-date information, making the overall analysis convincing and robust.

As regards the estimated number of workers exposed to cadmium and beryllium, the study concludes that the values considered by the external contractors for their modelling appear to be plausible and justified, based on the availability of data. However, the full current and future disease burden deriving from historic exposures to cadmium and beryllium is not captured, a weakness that is acknowledged in the IA.

This is a publication of the Ex-Ante Impact Assessment Unit (IMPA)
EPRS | European Parliamentary Research Service

This document is prepared for, and addressed to, the Members and staff of the European Parliament as background material to assist them in their parliamentary work. The content of the document is the sole responsibility of its author(s) and any opinions expressed herein should not be taken to represent an official position of the Parliament.

PDF ISBN 978-92-846-3464-4 | doi:10.2861/890113 | QA-06-18-276-EN-N