Committee for Risk Assessment (RAC)

Committee for Socio-economic Analysis (SEAC)

Opinion

on an Annex XV dossier proposing restrictions on:

Cobalt sulphate, Cobalt dichloride, Cobalt dinitrate, Cobalt carbonate and Cobalt di(acetate)

ECHA/RAC/RES-O-0000006741-74-01/F

ECHA/SEAC/[Opinion N°(same as opinion number)

Adopted

17 February 2020

17 February 2020

ECHA/RAC/RES-O-0000006741-74-01/F

12 March 2020

[SEAC opinion number]

Opinion of the Committee for Risk Assessment

and

Opinion of the Committee for Socio-economic Analysis

on an Annex XV dossier proposing restrictions of the manufacture, placing on the market or use of a substance within the EU

Having regard to Regulation (EC) No 1907/2006 of the European Parliament and of the Council 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (the REACH Regulation), and in particular the definition of a restriction in Article 3(31) and Title VIII thereof, the Committee for Risk Assessment (RAC) has adopted an opinion in accordance with Article 70 of the REACH Regulation and the Committee for Socio-economic Analysis (SEAC) has adopted an opinion in accordance with Article 71 of the REACH Regulation on the proposal for restriction of:

Cobalt sulphate
- CAS: 10124-43-3
- EC: 233-334-2

Cobalt dichloride
- CAS: 7646-79-9
- EC: 231-589-4

Cobalt dinitrate
- CAS: 10141-05-6
- EC: 233-402-1

Cobalt carbonate
- CAS: 513-79-1
- EC: 208-169-4

Cobalt di(acetate)
- CAS: 71-48-7
- EC: 200-755-8

This document presents the opinions adopted by RAC and SEAC and the Committee's justification for their opinions. The Background Document, which supports both the RAC and SEAC opinions and their justification, gives the details of the Dossier Submitters proposal amended with further information obtained during the consultation on the Annex XV report and other relevant information resulting from the opinion making process.

PROCESS FOR ADOPTION OF THE OPINIONS

ECHA has submitted a proposal for a restriction together with the justification and background information documented in an Annex XV dossier. The Annex XV report conforming to the requirements of Annex XV of the REACH Regulation was made publicly available at http://echa.europa.eu/web/guest/restrictions-under-consideration on **19 December 2018**. Interested parties were invited to submit comments and contributions by **19 June 2019**.

ADOPTION OF THE OPINION

ADOPTION OF THE OPINION OF RAC:

Rapporteur, appointed by RAC: ***Tiina SANTONEN***

Co-rapporteur, appointed by RAC: ***Urs SCHLÜTER***

The opinion of RAC as to whether the suggested restrictions are appropriate in reducing the risk to human health and/or the environment was adopted in accordance with Article 70 of the REACH Regulation on **17 February 2020** (by written procedure).

The opinion takes into account the comments of interested parties provided in accordance with Article 69(6) of the REACH Regulation.

The opinion of RAC was adopted **by consensus**.

ADOPTION OF THE OPINION OF SEAC

Rapporteur, appointed by SEAC: ***Simone FANKHAUSER***

Co-rapporteur, appointed by SEAC: ***Ivars BERGS***

The draft opinion of SEAC

The draft opinion of SEAC on the proposed restriction and on its related socio-economic impact has been agreed in accordance with Article 71(1) of the REACH Regulation **on 12 March 2020**.

The draft opinion takes into account the comments from the interested parties provided in accordance with Article 69(6)(a) of the REACH Regulation.

The draft opinion takes into account the socio-economic analysis, or information which can contribute to one, received from the interested parties provided in accordance with Article 69(6)(b) of the REACH Regulation.

The draft opinion was published at http://echa.europa.eu/web/guest/restrictions-under-consideration. Interested parties were invited to submit comments on the draft opinion by **25 May 2020**.

The opinion of SEAC

The opinion of SEAC on the proposed restriction and on its related socio-economic impact was adopted in accordance with Article 71(1) and (2) of the REACH Regulation on **[date of adoption of the opinion]**. **[**The deadline for the opinion of SEAC was in accordance with Article 71(3) of the REACH Regulation extended by **[number of days]** by the ECHA decision

[number and date]][1].

[The opinion takes into account the comments of interested parties provided in accordance with Article[s 69(6) and][5] 71(1) of the REACH Regulation.**] [**No comments were received from interested parties during the consultation in accordance with Article[s 69(6) and][3] 71(1)**]**[6].

The opinion of SEAC was adopted **by [consensus**.**][a simple majority]** of all members having the right to vote. [The minority position[s], including their grounds, are made available in a separate document which has been published at the same time as the opinion**.]**[6].

[1] Delete the unnecessary part(s)

Contents

OPINION OF RAC AND SEAC

The restriction proposed by the Dossier Submitter is:

Substance Identity (or group identity)	Conditions of the restriction
– Cobalt sulphate – CAS no 10124-43-3 – EC no 233-334-2 – Cobalt dichloride – CAS no 7646-79-9 – EC no 231-589-4 – Cobalt dinitrate – CAS no 10141-05-6 – EC no 233-402-1 – Cobalt carbonate – CAS no 513-79-1 – EC no 208-169-4 – Cobalt di(acetate) – CAS no 71-48-7 – EC no 200-755-8	1) Shall not be manufactured, placed on the market or used as substances on their own or in mixtures in a concentration equal or above 0.01% by weight, unless: a) if required by article 14 of REACH, registrants have carried out in their Chemical Safety Assessment an assessment according to paragraph 6.5 of Annex I of REACH and have used a reference exposure value of 0.01 µg Co/m^3 to demonstrate that all occupational exposures to the cobalt salts are below this reference level, and b) if required by article 37(4) of REACH, downstream users have carried out in their Downstream users Chemical Safety Assessment an assessment according to paragraph 6.5 of Annex I of REACH and have used a reference exposure value of 0.01 µg Co/m^3 to demonstrate all occupational exposures to the cobalt salts are below this reference level, and c) the supplier has provided the recipient of the substance on their own or in mixtures in a concentration equal or above 0.01% by weight with a Safety Data Sheet and exposure scenarios (where relevant) according to article 31 of REACH that includes the operational conditions and risk management measures to control occupational exposure to the cobalt salts below a reference exposure value of 0.01 µg Co/m^3. The Safety Data Sheet shall state the reference exposure value under Section 8.1 Control parameters. d) the manufacturers and downstream users have implemented a monitoring programme to ensure that all occupational exposures to the cobalt salts are below a reference exposure value of 0.01 µg Co/m^3 .[2] Paragraph 1 above shall not apply to the extent that the cobalt salts specified in column 1 are used as an additive in feedingstuffs within the scope of Regulation (EC) no 1831/2003 on additives for use in animal nutrition.

[2] See Appendix 1 of the Background Document for the calculation of exposure levels.

THE OPINION OF RAC

RAC has formulated its opinion on the proposed restriction based on an evaluation of the information related to the identified risk and to the identified options to reduce the risk as documented in the Annex XV report and submitted by interested parties as well as other available information as recorded in the Background Document. RAC considers that the proposed restriction on **Cobalt sulphate, Cobalt dichloride, Cobalt dinitrate, Cobalt carbonate and Cobalt di(acetate)** is the most appropriate Union wide measure to address the identified risk in terms of the effectiveness, in reducing the risk, practicality and monitorability as demonstrated in the justification supporting this opinion, provided that the conditions are modified, as proposed by RAC.

The conditions of the restriction proposed by RAC are:

Substance Identity (or group identity)	Conditions of the restriction
– Cobalt sulphate – CAS no 10124-43-3 – EC no 233-334-2 – Cobalt dichloride – CAS no 7646-79-9 – EC no 231-589-4 – Cobalt dinitrate – CAS no 10141-05-6 – EC no 233-402-1 – Cobalt carbonate – CAS no 513-79-1 – EC no 208-169-4 – Cobalt di(acetate) – CAS no 71-48-7 – EC no 200-755-8	1) Shall not be manufactured, placed on the market or used as substances on their own or in mixtures in a concentration equal or above 0.01% by weight, unless: a) if required by article 14 of REACH, registrants have carried out in their Chemical Safety Assessment an assessment according to paragraph 6.5 of Annex I of REACH and have used a limit value of 1 µg Co/m³ (as 8 h TWA, for the inhalable fraction) and 0.5 µg Co/m³ (as 8 h TWA, for the respirable fraction) to demonstrate that all occupational inhalation exposures to Cobalt sulphate, Cobalt dichloride, Cobalt dinitrate, Cobalt carbonate and Cobalt di(acetate) are below these limit values, and b) if required by article 37(4) of REACH, downstream users have carried out in their Downstream users Chemical Safety Assessment an assessment according to paragraph 6.5 of Annex I of REACH and have used a limit value of 1 µg Co/m³ (as 8 h TWA, for inhalable fraction) and 0.5 µg Co/m³ (as 8 h TWA, for respirable fraction) to demonstrate that all occupational inhalation exposures to Cobalt sulphate, Cobalt dichloride, Cobalt dinitrate, Cobalt carbonate and Cobalt di(acetate) are below these limit values, and c) the supplier has provided the recipient of the substance on their own or in mixtures in a concentration equal or above 0.01% by weight with a Safety Data Sheet and exposure scenarios (where relevant) according to article 31 of REACH that includes the operational conditions and risk

	management measures to control occupational inhalation exposure to thebelow a limit value of 1 µg Co/m³ (as 8 h TWA, for inhalable fraction) and 0.5 µg Co/m³ (as 8 h TWA, for respirable fraction). The Safety Data Sheet shall state the limit values under Section 8.1 Control parameters. d) the manufacturers and downstream users have implemented a monitoring programme to ensure that all occupational inhalation exposures to Cobalt sulphate, Cobalt dichloride, Cobalt dinitrate, Cobalt carbonate and Cobalt di(acetate) are below a limit value of 1 µg Co/m³ (as 8 h TWA, for inhalable fraction) and 0.5 µg Co/m³ (as 8 h TWA, for respirable fraction).

In addition, RAC considers it necessary, and proposes to the European Commission, to derive a binding occupational exposure limit value (BOELV) for cobalt and its compounds according to Directive 2004/37/EC on the protection of workers from the risks related to exposure to carcinogens or mutagens at work (CMD). RAC recommends that this value should be identical to the limit values given in this restriction. In addition to the inhalation exposure, manufacturers, importers and users of the cobalt compounds should pay attention to the prevention of exposure via the skin.

THE OPINION OF SEAC

See the opinion of SEAC.

JUSTIFICATION FOR THE OPINION OF RAC AND SEAC

IDENTIFIED HAZARD, EXPOSURE/EMISSIONS AND RISK

Justification for the opinion of RAC

Description of and justification for targeting of the information on hazards and exposure/emissions (scope)

Summary of proposal:

This restriction concerns the placing on the market, manufacture and use of five water soluble cobalt salts: cobalt sulphate, cobalt dichloride, cobalt dinitrate, cobalt carbonate and cobalt di(acetate) on their own or in mixtures in a concentration equal to or above 0.01% by weight in industrial and professional applications. Further referred to as 'five cobalt salts' under in this opinion, they have a harmonised classification as Carc 1B and Muta 2. Consumer uses are not expected and are therefore outside the scope of this restriction. The current use of these cobalt salts in the EU is 30 000 tonnes per year with the highest amounts used as transported isolated intermediates for the manufacturing of other chemicals. The volumes are expected to rise in future due to the increasing demand for rechargeable batteries and biotechnology-health applications. It has been estimated that 35 000 workers at around 20 000 industrial sites are exposed to the five cobalt salts.

ECHA made an assessment on the uses of cobalt salts in 2017 and using the RAC dose response for carcinogenicity (2016) calculated excess cancer risks in all sectors involving exposure to these cobalt salts in the range of 10^{-3} to 10^{-2}. Based on these findings, the European Commission requested ECHA to prepare an Annex XV restriction dossier covering these five cobalt salts and addressing risks at the workplace. In the current restriction dossier, the Dossier Submitter identified that cancer risks to workers are currently not adequately controlled and that risk management is required at the Union level.

These five cobalt salts are grouped since they have similar bioaccessibility and bioavailability properties, resulting in similar release of cobalt ions. The cobalt (II) ion is considered responsible for the carcinogenicity of cobalt. The Dossier Submitter notes that cobalt metal and several other poorly water-soluble compounds (e.g. cobalt oxide) have also been found to be soluble in biological fluids and can release cobalt (II) ions *in vivo*. Therefore, these cobalt compounds could also cause risks that might be addressed by this restriction proposal. However, due to the specific request of the Commission, this restriction has been limited to the five named cobalt salts.

RAC conclusions:

RAC conclusions on the scope:

- Cobalt (II) ions released in biological fluids from cobalt metal and cobalt compounds are recognised as the source of toxicity in humans. At the request of the Commission, the Dossier Submitter developed a restriction under the REACH regulation on the five registered soluble cobalt salts; this limited the scope of the restriction. RAC points out that not including other cobalt compounds in the scope has implications for the protection of workers, which are further discussed in the section on "justification whether the suggested restriction is the most appropriate EU wide measure". One

aspect – as identified by the Dossier Submitter – to note is that in occupational settings, possible co-exposure to different cobalt compounds may also make it difficult to monitor the exposure to the restricted cobalt salts only. **RAC supports the restriction targeted at the five soluble cobalt salts, but additionally recommends to the European Commission to derive a binding occupational exposure limit value (BOELV) for cobalt and its compounds according to directive 2004/37/EC on the protection of workers from the risks related to exposure to carcinogens or mutagens at work (CMD).**

- The current restriction proposal is targeted at **lung cancer risk**, which is dependent on cumulative working life exposure and is therefore meant to be adjusted for the frequency and duration of exposure. However, when exposure is averaged over the whole year, infrequent peak exposures may remain uncontrolled. These short term higher exposures are likely to be relevant for cobalt sensitisation and other non-cancer (respiratory) effects and the limit value should also be protective for these effects.

- The current restriction proposal concerns an air limit value and as such does not protect from skin sensitisation. In order to protect workers from the risk of skin sensitisation, risk management measures at the workplaces are needed for the prevention of skin exposure.

Key elements underpinning the RAC conclusion:

See further justifications in the following sections.

Description of the risks addressed by the proposed restriction

Information on hazards

Summary of proposal:

The hazard property on which this restriction is based is carcinogenicity. The five cobalt salts in the scope of this proposed restriction have a harmonised classification under the CLP regulation as: Carc. 1B (H350, may cause cancer) and Muta 2 (H341, suspected of causing genetic defects). In addition, they are classified as category 1 skin and respiratory sensitisers (H317, may cause an allergic skin reaction; H334, may cause allergy or asthma symptoms or breathing difficulties if inhaled).

It is assumed that the carcinogenicity and mutagenicity of cobalt compounds in general is driven by the cobalt (II) ions, which are released in the body. The Dossier Submitter's proposal on the dose-response of the carcinogenicity of cobalt salts is based on the RAC opinion from 2016. Since the human data on the carcinogenicity of cobalt is limited, the dose response is based on experimental data from animals, i.e. on the lowest BMDL10 value of 0.414 mg/m³ that was found for female rat tumours in NTP (1998) inhalation studies, in which mice and rats were exposed to cobalt sulphate heptahydrate by inhalation. A linear approach was used to derive the following dose-response for occupational exposure to respirable cobalt:

Excess risk (lung cancer, workers) = 1.05 x exposure level (as mg Co/m^3, respirable fraction)

Cobalt salts were assessed using a non-threshold approach because of the lack of identified

thresholds and the uncertainties regarding the mechanisms involved. Although it was recognised that inhalable particles also produce pre-malignant lesions (hyperplasia, metaplasia and atrophy) in animal studies, and therefore inhalable particles should also be considered as carcinogenic, it was not possible to derive a dose-response related to this fraction and the dose-response was therefore derived only for the respirable fraction.

However, the Dossier Submitter considered it appropriate to apply the dose–response relationship derived for lung cancer to characterise all cancer effects (local and systemic) resulting from inhalation exposure to the cobalt salts since it was not possible to exclude systemic and local carcinogenicity effects resulting from the deposition of particles to upper respiratory tract and ingestion and/or absorption of cobalt. In animal experiments, cobalt sulphate inhalation caused a statistically increased incidence of pheochromocytomas at the highest dose in females. In males, a significant increase was seen only at the second highest dose, i.e. no dose response was seen. Since this was the only evidence on systemic tumours after exposure to soluble cobalt salts, RAC (2016) did not consider this evidence strong enough and concluded that cobalt salts are local carcinogens. However, inhalation studies with cobalt metal (see RAC opinion on the classification of cobalt metal, 2017) indicated neoplasms at several organ sites (pancreas, adrenal gland, hematopoietic system and kidney) which was considered to support the systemic carcinogenicity of cobalt.

Since the RAC (2016) opinion, two epidemiological studies have been published on the cancer risk caused by cobalt compounds (Sauni et al., 2017 and Marsh et al., 2017). Summaries of both studies have been included in the dossier but the Dossier Submitter did not consider them to have an impact on the hazard characterisation. Neither of the studies provided any consistent evidence of increased cancer risk in humans.

The Dossier Submitter has presented an overview on the skin and respiratory sensitisation properties of the cobalt salts but has not quantified the hazard. According to the Dossier Submitter the conditions of the proposed restriction will lead to a reduction in occupational exposure that will result not only in a reduction of cancer cases but also in the prevention of new cases of skin and respiratory sensitisation among the exposed workers.

RAC conclusions:

- While RAC (2016) states in its conclusions that "*the cobalt salts may be considered genotoxic carcinogens using a non-threshold approach for risk assessment*" it also acknowledges that "*the current scientific findings and mode of action considerations support the notion that water soluble cobalt substances may be threshold carcinogens although there are some uncertainties related to initiation by catalytic ROS generation and direct oxidative DNA damage*". Because of these threshold mechanisms, the use of a linear approach for dose-response is considered by RAC to be very conservative and is likely to result in the overestimation of risks especially at lower exposure levels (acknowledged also by RAC 2016 and agreed again during the opinion development of this restriction proposal).

- RAC chose to assess whether a mode of action-based threshold for cancer effects could be derived for cobalt following the methodology of the ECHA/RAC – SCOEL Joint Task Force (ECHA, 2017), which was recently added as an Appendix to ECHA R.8 Guidance (ECHA, 2019). However, it was concluded that the data was insufficient to derive such a health-based threshold. As a result, other options were assessed.

- RAC acknowledges that chronic inflammation is likely to play a role in the mode of action of cobalt-caused genotoxicity and cancer. An estimated threshold level for chronic pulmonary inflammation of **0.5 µg Co / m³ (respirable fraction)** is derived using animal data. This can be considered to present a breakpoint in the dose-response of cobalt carcinogenicity. It needs to be stressed, that due to the gaps in the knowledge about the carcinogenicity of cobalt, this cannot be identified as a health-based (fully safe) threshold below which cancer risks can be considered negligible. However, below this level, the cancer risk is likely to be reduced significantly compared to the risk estimated on the basis of linear extrapolation. Since inflammation and secondary genotoxicity at levels >0.5 µg/m^3 may enhance the cancer risk, the levels should be controlled below the breakpoint as an 8 h time weighted average (TWA) rather than a frequency and duration-adjusted reference exposure value (the latter as proposed by the Dossier Submitter).

- The use of the dose–response relationship derived for lung cancer to characterise other (upper respiratory tract and systemic) cancers is an additional conservative assumption made by the Dossier Submitter. As noted by RAC (2016), hyperplasia, metaplasia and atrophy in epithelial cells of the nose, and metaplasia of the squamous epithelium of the larynx, were seen in long-term animal studies at the highest dose. However, neither epidemiological nor animal studies have provided evidence of upper respiratory tract tumours. Therefore, RAC (2016) concluded that no dose-response can be derived for inhalable particles. In animal studies >40% of the respirable particles are expected to deposit in the head region (see the discussion under "key elements underpinning RAC's opinion) whereas about 4% end up to alveolar region. When taking into account the absence of tumours in the upper respiratory tract at the highest concentration tested (3.0 mg/m^3 cobalt sulphate hexahydrate) whereas already 0.3 mg/m^3 concentration resulted in increased incidence of pulmonary tumours, the risk of upper respiratory tract cancers is more than one order of magnitude lower than that of lung cancer. Even though in animal studies pheochromocytomas and pancreatic cancers were observed after the inhalation exposure to cobalt metal, the relevance of these systemic cancers to low level human exposures is unclear. As concluded by RAC in its opinion on the classification and labelling of cobalt metal (2017), the mechanisms of these cancers may be related to the high doses used in animal studies and may exert a threshold. Because of the clear potency difference (1-2 orders of magnitude), dose response for respirable particles is considered to cover also possible cancer risk caused by the non-respirable particles. Thus, applying the lung cancer dose-response to characterise the risk of other cancers caused by non-respirable cobalt dust is not considered appropriate from a toxicological point of view.

- The new large epidemiological study by Marsh et al (2017) from hard metal production does not show increased cancer risk associated with cobalt exposure in humans. However, based on this study it can only be concluded that humans are at least not more sensitive to cobalt than animals.

- The Dossier Submitter did not perform a quantitative hazard assessment for the other toxicological effects of cobalt, including respiratory sensitisation and other non-cancer lung effects as they were considered to be covered by the proposed reference exposure value. Although the quantitative dose-response data on the non-cancer lung effects

are limited, the data by Nemery et al., 1992 suggests that at levels below 5 µg Co/m³ there is no effect on lung function in exposed workers. Based on this, **a limit value of 1 µg Co/m³ for the inhalable fraction** can be set by using an assessment factor (AF) of 5 for inter-individual differences. Although, the current data do not allow setting of a NOEC for asthma, based on the data available from three Member States and from an industry survey, asthma caused by cobalt seems to be uncommon nowadays. It is agreed by RAC that the limit value given above is likely to reduce the risk of respiratory sensitisation as well. Since cobalt sensitisation may be more related to daily exposure levels rather than cumulative exposure, this value should be used as an 8 h TWA value rather than a frequency- and duration-adjusted reference exposure value. Since an air limit value alone cannot protect from skin sensitisation, careful control of skin exposure at workplaces is also needed to protect workers from the risk of skin sensitisation.

Key elements underpinning the RAC conclusions:

Lung cancer

RAC evaluated the carcinogenicity of cobalt salts in 2016. That evaluation included the consideration of the mode of action of cobalt, which has an impact on the shape of the dose response for carcinogenicity. Cobalt salts (and elemental cobalt) do not cause direct mutagenicity, but have been shown to cause DNA damage as displayed in Comet assays, chromosomal aberrations and micronuclei *in vitro*. *In vivo*, genotoxicity has been observed mainly after intraperitoneal administration. There are several studies which suggest that the main mechanisms of cobalt induced genotoxicity are induction of reactive oxygen species (ROS) and oxidative stress, inhibition of DNA repair and stabilisation/up-regulation of hypoxia-inducible factor (HIF-1α). The ToxTracker data (Hendricks et al., 2019) submitted during the consultation supports the role of oxidative stress and HIF-1α in the mode of action of cobalt. Chronic inflammation observed in animal inhalation studies at the levels causing carcinogenicity is likely to play a role in the genotoxicity of cobalt resulting in secondary genotoxicity via ROS production and oxidative damage. RAC concluded in its earlier assessment (RAC, 2016) that the current scientific findings and mode of action considerations support the notion that water soluble cobalt salts may be threshold carcinogens, given that inflammation and the main mechanisms of cobalt-induced genotoxicity are threshold events. However, RAC considered at that time that there are remaining uncertainties (as to e.g. the possibility of non-threshold mechanisms for genotoxicity and whether inflammation is a prerequisite for the carcinogenicity) and that the data is not sufficient to *identify* a threshold level for the genotoxicity and carcinogenicity of cobalt. Therefore, residual cancer risk at low exposure levels could not be totally excluded. This resulted in the selection of a non-threshold approach for the dose-response analysis: a BMDL10 of 0.414 mg/m^3 as cobalt sulphate hexahydrate (0.093 mg/m^3 as cobalt) based on lung tumours in rat inhalation carcinogenicity study (NTP, 1998) was selected as a point of departure for linear extrapolation. For workers, this resulted in a dose-response of 1.05 (mg/ Co/m^3)$^{-1}$ x exposure concentration for excess lung cancer risk (respirable fraction). It was, however, emphasised that this is a very conservative approach, which is likely to result in the overestimation of risks especially at lower exposure levels.

Human data on the carcinogenicity of cobalt and its compounds does not provide clear evidence on the carcinogenicity of cobalt. Since RAC's (2016) evaluation, there are two new studies published (Sauni et al., 2017 and Marsh et al., 2017), which should be considered. Sauni et al (2017) evaluated the cancer incidence among workers (995 males) employed in

a Finnish cobalt plant. No clear association between cancer risk and exposure was found. However, the study size was small. Marsh et al (2017) is the most recent study on the association between cancer and cobalt exposure. It concerns hard metal production and includes >30 000 exposed workers. Even though the study was related to the hard metal industry (production and processing of hard metal, e.g. cemented carbide), it is still considered relevant for cobalt salt assessment since also metallic cobalt releases cobalt ions in biological fluids and according to animal data the carcinogenic potency of cobalt and cobalt salts is rather similar in animals. The study did not show a clear association between cancer and cobalt exposure as increased risks for lung cancer was seen only in short-term workers (<1 y of exposure) and no dose-response with cumulative or mean cobalt exposures was seen. The highest exposure category in this study had cumulative exposure of >0.1275 mg/m^3-years, which can be calculated to correspond an average of 0.003 mg/m^3 exposure for 40 years. At this exposure level the dose-response results in a lung cancer incidence of three extra cases / 1 000 exposed. This number of excess cancers derived from animal studies corresponds to a risk ratio of approximately 1.3 in humans. Naturally, some of these workers in the high exposure group may have been exposed to higher levels than 0.1275 mg/m^3-years. However, based on this study it can be only concluded that humans are at least not more sensitive to cobalt than animals.

Overall, human data have not shown any clearly increased cancer risk in occupationally exposed workers. This cannot, however, be used to exclude the cancer risk seen in animal studies. Neither does it provide additional information on a potential threshold for carcinogenicity. Thus, the quantification of cancer risk needs in the case of cobalt to be based on animal data.

In 2017, the RAC-SCOEL Joint Task Force (JTF) agreed on the concept of identifying mode of action based thresholds for genotoxic carcinogens if there is robust evidence of indirect genotoxicity and of the mode of action, and the data allow setting a threshold for the main mode of action (if not, the non-threshold approach is the default). An update of ECHA R.8 Guidance on dose-response includes a description of this concept (ECHA, 2019). This mode of action based threshold approach has been applied by RAC for inorganic nickel compounds[3], benzene[4] and acrylonitrile[5]. For the present evaluation, RAC therefore examined the applicability of a mode of action based threshold approach for cobalt salts, as the mechanistic data (discussed in detail in the 2016 RAC evaluation) suggests that the dose-response of cobalt carcinogenicity may include a mode of action based threshold. With this in mind, the available data for cobalt was compared to that on inorganic nickel compounds. It can be concluded that regarding an *in vitro* mode of action, data on the genotoxicity of cobalt can be considered comparable to that for nickel. However, in contrast to nickel, there is no *in vivo* dose response data on the local genotoxicity of cobalt nor data allowing the derivation of N(L)OAECs for these genotoxic effects in relation to the N(L)OAECs for pulmonary

[3] Opinion on scientific evaluation of occupational exposure limits for Nickel and its compounds ECHA/RAC/A77-O-0000001412-86-189/F https://echa.europa.eu/documents/10162/13641/nickel_opinion_en.pdf/9e050da5-b45c-c8e5-9e5e-a1a2ce908335

[4] Opinion on scientific evaluation of occupational exposure limits for Benzene ECHA/RAC/ O-000000-1412-86-187/F https://echa.europa.eu/documents/10162/13641/benzene_opinion_en.pdf/4fec9aac-9ed5-2aae-7b70-5226705358c7

[5] Opinion on scientific evaluation of occupational exposure limits for Acrylonitrile ECHA/RAC/O-0000001412-86-188/F https://echa.europa.eu/documents/10162/13641/acrylonitrile_opinion_en.pdf/102477c9-a961-2c96-5c4d-76fcd856ac19

inflammation. This is considered a crucial difference since even though it is likely that chronic inflammation contributes to the genotoxicity and carcinogenicity of cobalt, genotoxic effects at the levels below the threshold for inflammation cannot be totally excluded. The lack of crucial data for cobalt precludes a mode of action based threshold to be identified. In principle, the non-threshold approach as proposed by the Dossier Submitter would thus be the default approach for cobalt.

However, RAC reiterates the very conservative nature of this approach, especially at very low exposure levels, and considers it likely that the dose-response curve in the lower exposure range is less steep than in the higher range. To better reflect this, RAC chose the sublinear approach introduced by AGS (TRGS 910, 2014) as an alternative, with lung inflammatory effects as the marker for the breakpoint in the dose-response for the genotoxicity and carcinogenicity of cobalt. Chronic inflammation is known to result in oxidative stress and to exaggerate DNA damage. Cobalt-induced inhibition of repair of DNA damage may further exaggerate genomic instability. Below the level for inflammation, remaining cancer risk cannot to be totally excluded (given the uncertainties surrounding any mode of action based threshold), but the cancer risk is likely to be reduced compared to the risks calculated on the basis of linear extrapolation since inflammation-related mechanisms do not play a role anymore.

In the mouse and rat inhalation carcinogenicity studies (NTP, 1998), inflammation was observed with very high incidences at all concentrations tested (0.3, 1 and 3 mg/m³ as cobalt sulphate hexahydrate). In the absence of a NOAEC for inflammatory effects for cobalt, the LOAEC of 0.3 mg/m³ as cobalt sulphate hexahydrate, corresponding to 0.067 mg/m³ as cobalt, was taken as the point of departure for calculating the exposure concentration representing the breakpoint in the dose-response curve. Following conversion of the point of departure into a worker equivalent dose of 0.034 mg/m³ (= 0.067 mg/m³ * 6h/8h * 6.7 m³/10 m³) and applying assessment factors of:

- 2.5 for remaining interspecies differences,
- 5 for worker intra-species differences, and
- 5 for dose-response/severity,

A reference exposure value of 0.00054 mg Co/m³ (rounded as 0.0005 mg Co/m³) can be derived for the respirable fraction. In the absence of cobalt-specific data informing on the degree of cancer risk reduction below this exposure value, RAC took a 10-fold lower cancer risk as a default (cf. AGS, 2014). Applying this approach, at exposure levels ≤0.0005 mg Co/m³ the dose-response for excess lung cancer risk for workers becomes 0.105x the exposure concentration (as mg Co/m³, respirable fraction). The remaining cancer risk in this lower exposure range can be considered as being below 5.25×10^{-5}. For exposure levels >0.0005 mg Co/m³ the dose-response for excess lung cancer risk for workers becomes steeper, 1.0576x the exposure concentration (as mg Co/m³, respirable fraction) - 0.0004763.

Human data, suggesting LOAECs for non-cancer pulmonary effects at levels > 0.01 mg/m³ (as inhalable dust) and a NOEAC of 0.005 mg/m³ can be used as supporting evidence and for the setting of a limit value for inhalable dust (for further description of this data see paragraph "*Chronic non-cancer lung effects and respiratory sensitisation*").

Upper respiratory tract carcinogenicity

Neither epidemiological studies nor animal studies have provided evidence of upper respiratory tract tumours. In animal studies with mice and rats (NTP, 1998), no tumours were seen at the highest concentration (3.0 mg/m^3 cobalt sulphate hexahydrate, = NOAEL for carcinogenicity in upper respiratory tract) whereas already 0.3 mg/m^3 resulted in increased incidence of pulmonary tumours both in mice and rats (=LOAEL for carcinogenicity in the lungs). However, the results indicated that both rats and mice develop hyperplasia, metaplasia and atrophy in epithelial cells of the nose, and metaplasia of the squamous epithelium of the larynx suggesting potential carcinogenicity in the upper respiratory tract.

Since no cancers were observed, it is not possible to derive a dose-response for the upper respirable tract cancers. This was concluded also by RAC (2016) (*"Although inhalable particles should also be considered as carcinogenic the dose-response related to this metric is far more uncertain as this will very much depend of the content of respirable particles. Thus, the most valid dose-response relationship for carcinogenicity is to be based on an exposure metric for respirable particles."*). These data, however, show that the upper respiratory tract is more than one order of magnitude less sensitive to the carcinogenic effects of cobalt compared to the lower respiratory tract.

When doing this kind of comparison, particle deposition to the different regions of the respiratory tract should be taken into account. Even though the median mass aerodynamic diameter (MMAD) of cobalt sulphate particles was in the respirable range (MMAD ± GSD 1.4-1.6 ± 2.1-2.2), considerable amounts of particles are also deposited in the upper respiratory tract. Multiple path particle deposition (MPPD) models can be used to estimate the deposited fractions in the different regions of the respiratory tract (AGS, 2013). Using the particle size distribution from the NTP (1998) studies, EBRC (2016) used an MPPD model to calculate that 44.2% of the particles are deposited in the upper respiratory tract in rats, 1.5% in the tracheobronchial region and 4.3% in pulmonary region. Thus, at the level of 0.67 mg Co/m^3 (NOAEL for upper respiratory tract tumours), a dose of 0.3 mg Co/m^3 was deposited to the upper respiratory tract (head) and 0.03 mg Co/m^3 was deposited in the alveolar region. When taking into account that increased cancer incidence in the alveolar region was observed already at a 10-fold lower concentration than the NOAEL for upper respiratory tract tumours, it suggests that the sensitivity of rat upper respiratory tract is one to two orders of magnitude lower than the sensitivity of lower respiratory tract. Because of the clear potency difference, the dose response for respirable particles is considered to cover also possible cancer risk caused by the non-respirable particles. Therefore, applying a lung cancer dose-response for upper respiratory tract tumorigenicity on the basis of animal data is not considered scientifically justified.

Systemic carcinogenicity

Carcinogenicity studies with soluble cobalt salts have not shown clear evidence of systemic cancers (RAC, 2016). The concern for systemic carcinogenicity has mainly been raised from the studies with cobalt metal, in which increased incidences of systemic cancers were seen in rats (but not in mice). Detailed descriptions of these studies have not been included in the Background Document but, as discussed in the RAC opinion on the classification and labelling of cobalt metal (2017), the main tumour types that increased in rats (but not in mice) after exposure to cobalt dust were pheochromocytomas and pancreatic cancers. Mononuclear cell leukaemia (MNCL) incidence was increased at all doses without a clear dose-response and

kidney cancers were increased in male rats at the highest dose level exceeding MTD.

Increased incidence of pheochromocytomas at high doses has been linked to lung damage associated hypoxia and cobalt promotion of a hypoxia-like state even with normal molecular oxygen pressure by stabilising hypoxia-inducible factor (HIF-1α), which is a major regulator of the adaptation of cancer cells to hypoxia. Also insoluble nickel metal (but not other nickel compounds) has caused similar increases in the incidence of pheochromocytomas at high doses, which were considered to be related to hypoxia rather than to systemic nickel levels (ECHA, 2018[6]).

If lung damage is considered as the main mechanism for pheochromocytomas in rats, the relevance of these tumours at lower exposure levels can be considered negligible. In addition, effects mediated via the activation of HIF-1α can be considered to exert a threshold. Another tumour type increased in male rats (but not in females or in mice) was pancreatic islet tumours. Increase in this tumour type has not been seen with soluble cobalt salts. Also in this case, a mechanism related to the hypoxia-mediated oxidative stress and facilitation of the growth of neoplasm by the degradation of oncogene MUC4 has been proposed (Joshi, 2016[7]). Thus, there are indications that these effects might not be relevant at lower dose levels. In addition, if the limit value for cobalt is set at 1 µg Co/m^3 inhalable fraction and 0.5 µg Co/m^3 respirable fraction, the systemic cobalt levels are likely to stay close to background levels seen in occupationally non-exposed general population (see Appendix 7 of the Background Document on the biomonitoring of cobalt).

Chronic non-cancer lung effects and respiratory sensitisation

The dossier includes a chapter on sensitisation but no quantitative assessment of sensitisation (respiratory or skin sensitisation) or other non-cancer lung effects has been made. Non-cancer lung effects in animals have been described in the paragraph “Lung cancer”. There are only a few published studies which give some dose-response data on the non-cancer pulmonary effects in humans. Studies by Roto et al (1980[8]) and Swennen et al (1993[9]) reported effects on lung function at 0.1 mg/m³. Linna et al., (2003[10]) did not see effects on lung function in a cobalt salt manufacturing plant at an average cumulative exposure level of 1 mg/m³-years (since the average exposure duration was 22 years, the average exposure level in this study was ~0.045 mg/m³). Nemery et al., (1992[11]), on the other hand, showed lung function effects in diamond polishers already at an exposure level of 0.015 mg Co/m³. They identified a NOAEC of 0.0053 mg Co/m³ for lung function impairment in these workers. This NOAEC has been used e.g. by IPCS 2006 (CICAD 69, cobalt and inorganic cobalt compounds[12]) for the setting of a limit value for inhalation exposure. The workers may also have been exposed to occasional traces of other elements (copper, zinc, titanium, manganese, chromium, silicon dioxide and silicates, as well as iron) formed in diamond polishing. Nevertheless, the authors considered cobalt to be the only relevant exposure in these workshops. Verougstraete et al (2004[13]) demonstrated effects on lung function only in cobalt exposed smokers in a cobalt

[6] ECHA (2018) Committee for Risk Assessment (RAC) Opinion on scientific evaluation of occupational exposure limits for Nickel and its compounds ECHA/RAC/ A77-O-0000001412-86-189/F and its annexes. Adopted 9 March 2018.
[7] Joshi et al., Oncogene. 2016 Nov 10;35(45):5882-5892. doi: 10.1038/onc.2016.119.
[8] Roto, Scand J Work Environ Health. 1980;6 Suppl 1:1-49
[9] Swennen et al, Br J Ind Med. 1993 Sep;50(9):835-42
[10] Linna et al., Am J Ind Med. 2003 Aug;44(2):124-32.
[11] Nemery et al. Am Rev Respir Dis. 1992 Mar;145(3):610-6.
[12] https://www.who.int/ipcs/publications/cicad/cicad69%20.pdf

[13] Verougstraete et al., Am J Respir Crit Care Med. 2004 Jul 15;170(2):162-6

manufacturing plant. The exposure level in the highest exposure group in this study was 0.04 mg/m³.

These human studies give information on the non-cancer lung effects in relation to inhalable cobalt dust levels at workplaces. If the standard AF of 5 is applied to the NOAEC of 0.005 mg/m³ (from Nemery et al., 1992) to account for the inter-individual differences, a limit value of 0.001 mg/m³ is derived for inhalable cobalt dust. Noting that the respirable fraction usually represents ≤50% of inhalable dust, a value of 0.001 mg/m³ is in accordance with the breakpoint level of 0.0005 mg/m³ derived for respirable dust on the basis of animal data providing additional support for the latter value.

The five cobalt salts covered by this restriction proposal have a harmonised classification as Resp. Sens. 1 as well as Skin Sens. 1 according to CLP. There are human data on the occupational asthmas caused by cobalt. However, data on the underlying dose-responses are limited.

Roto et al (1980) concluded that cobalt asthmas may occur already at exposure levels of <0.1 mg/m³ based on his study in cobalt salt manufacturing. Subsequently, Sauni et al (2010[14]) made an evaluation of the asthma cases diagnosed in the same cobalt salt manufacturing plant and concluded that exposure to cobalt sulphates in the department with average exposures of 0.03 mg/m³ (range 0.01-0.1 mg/m³) still resulted in an asthma incidence density (number of new cases per person-years) of 0.005. The total number of cobalt asthmas diagnosed between 1967 and 2003 in the plant was 22. This is the only study giving some dose-response information on asthma risk due to cobalt salts. Asthma in these cases could have been exaggerated by the co-exposure to sulphur dioxide, since in the chemical department with exposure to different cobalt species at the level of 0.12 mg/m³ (0.02-0.3 mg/m³) no asthma cases were identified. A study from a hard metal factory supports that cobalt asthmas may be caused by mean TWA exposures of <0.05 mg/m³ (Kusaka et al., 1986[15]). However, on the basis of these data it is not possible to set a threshold for cobalt respiratory sensitisation.

According to the information received by the Dossier Submitter from three Member States (representing approximately 3% of the population of the EU), there are one to three registered cases per year of occupational skin diseases and zero to one cases of asthma due to occupational exposure to cobalt. The information does not distinguish among exposures to different cobalt compounds. During consultation, the Cobalt REACH Consortium provided information on their survey on cobalt sensitisation cases. The number of asthma cases reported in the last 10 years by the companies participating in the survey was zero. The number of skin sensitisation cases was reported as less than 0.5 cases per year. Similarly, the number of cases reported results from exposure to cobalt and cobalt compounds and cannot be related to the specific cobalt compounds covered by the restriction proposal.

Frequency adjustment of the proposed limit value

The reference exposure value (REV) proposed by the Dossier Submitter is a frequency- and duration-adjusted limit value. Asthma risk may, however, be more related to high short-term exposures. In activities occurring infrequently, a frequency- and duration-adjusted reference value of 1 µg/m³ may allow short term exposures (≥0.03-0.1 mg/m³), which have been

[14] Sauni et al., Occup Med (Lond). 2010 Jun;60(4):301-6.
[15] Kusaka et al., Br J Ind Med. 1986 Jul;43(7):474-85.

associated to the occurrence of asthma. In addition, a frequency adjusted REV may allow 8 h exposures above the breakpoint, which may result in inflammation and secondary genotoxicity. Therefore, if the breakpoint level of 1 µg Co/m³ (inhalable fraction)/0.5 µg Co/m³ (respirable fraction) is applied as a limit value it should be used as an 8 h TWA level rather than a frequency and duration-adjusted reference value.

Other evaluations

The Dossier Submitter did not include an overall appraisal of the risk assessments performed by other bodies in the Annex XV restriction report, although summaries of the assessments were included in Annex B. Assessments published before 2016 have also been summarised in RAC (2016). Inflammation was considered a critical endpoint by the French Agency for Food, Environmental and Occupational Health & Safety (ANSES) who established a pragmatic Occupational Exposure Limit (OEL) of 0.0025 mg Co/m³ based on BMDL10 of 0.07 mg/m³ (as cobalt) for inflammation in rats exposed to cobalt sulphate hexahydrate. OECD (2014) and REACH CSR considered carcinogenicity of the Co to include a threshold and considered the BMDL10 for cancer effects in animals as a suitable point of departure for the risk assessment. The German MAK Commission (Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area) concluded in 2007/2009 that no threshold could be derived for genotoxicity and cancer. Other assessments performed earlier (like IPCS 2006 cited above) based their limit values to other health effects (non-cancer lung effects like irritation or reduced lung function in humans).

Information on emissions and exposures

Summary of proposal:

Production volumes and sectors of use

The five cobalt salts are manufactured in and imported into the EU, and used in a wide range of sectors and applications. The total volume manufactured and imported is estimated at 37 400 tonnes/year (30 000 are used in the EU and 7 400 are exported). Approximately 85% of the cobalt salts are used as intermediates in the EU; 70% of the total volume is used as transported isolated intermediates. Table 1 below shows the sectors of use of the cobalt salts and the corresponding volumes for each sector.

Table 1: Estimated annual volume of cobalt salts by sector of use

Sector / Uses	Volume used in EU (tonnes 2011-2013)
Intermediate uses	
Manufacture of chemicals and batteries	26 600
Manufacture of catalysts	1 700
Manufacture of pigments and dyes	<<100
Non-intermediate uses	
Use as catalyst	700
Use in surface treatment (incl.: formulation, passivation and plating)	500
Use in biotechnology (incl. biogas, fermentation, health sector, animal feed and fertilizers)	400
Bespoke uses (incl. humidity indicators card, water treatment chemicals, laboratory reference standards)	<<100
Total	30 000

Source: Data extracted from information provided by the Cobalt Institute in the call for evidence for the

preparation of this restriction dossier (Cobalt REACH Consortium Ltd., 2017)

Worker exposure

Workers may be exposed to the five cobalt salts in the manufacture and use of the substances via the inhalation, dermal and (potentially) oral route. The focus of the restriction dossier is on the worker inhalation exposure. Dermal exposure (and potential oral exposure) is only briefly reported by the Dossier Submitter.

According to the registration dossiers, the cobalt salts are prepared and used as solids in powder form with a medium dustiness. Some of the processes, (e.g. in animal feed, manufacture of catalysts, etc.) result in the transformation of the cobalt salts into dry solids (cakes, granules, pellets, etc.) with a lower potential for dust emission.

The five cobalt salts (except for cobalt carbonate) are also produced and used in liquid form, mainly as aqueous solutions. The use of aqueous solutions can lead to the generation of mists and fumes in high energy activities such as electroplating and hot metallurgical processes.

Particle size distribution

The particle size distribution of the aerosols (dust, fumes and mists) generated during manufacture and use is a key parameter in the occupational exposure to cobalt salts:

- Larger particles (> 100 µm in diameter) deposit easily and their contribution to inhalation exposure is less relevant.
- Smaller particles tend to become air-borne and are inhalable (> 10 µm) or even respirable (< 10 µm).

According to industry, the ratio of the inhalable to respirable fraction for the five cobalt salts can be estimated at 10:1 (10% respirable dust) as a reasonable worst case, based on a report containing detailed particle size information from three workplaces (Vetter et al., 2016).

The Dossier Submitter considers that a fraction of 10% of respirable cobalt particles does not take into account the different scenarios where exposure to the cobalt salts may occur. Instead, based on a study conducted by Okamoto (1998), the Dossier Submitter proposes a ratio of two (50% respirable dust) as the reasonable worst case for the respirable fraction for cobalt salt particles.

Nevertheless, as discussed in section 1.2.4.2 of the Background Document, the Dossier Submitter proposed to apply the dose-response (derived for the respirable fraction) to the inhalable fraction as a preventive approach to take into account also the carcinogenicity effect of the non-respirable fraction.

Inhalation exposure

Air monitoring data, as presented in the registration dossiers (Cobalt REACH Consortium Ltd., 2018), are the basis for the exposure assessment of the Dossier Submitter. These data were obtained from a number of workplaces where cobalt and/or cobalt compounds are manufactured and handled. The measured values are based on personal sampling. The median value is reported for those sectors where it is available. The Reasonable Worst Case (RWC) is based on the 90th percentile unless otherwise stated. The values shown correspond to the activities within the sector showing the highest exposure levels in the exposure

scenarios, excluding cleaning and maintenance. For intermediate uses, only activities where the cobalt salts are present are considered, i.e. before they are transformed into other substances.

The initially available data set has a number of limitations which are identified by the Dossier Submitter and introduces a significant level of uncertainty to the analysis:

- Exposure levels of cobalt are in most cases reflective of parallel exposure to a variety of cobalt substances and not only relevant for the five cobalt salts within the scope.

- The number of available measurements is still unclear to some extent, despite the efforts made by the Dossier Submitter who was able to provide information about the number of measurements. However, it is only known that for some exposure scenarios the number of measurements available is very low e.g.:
    - For the surface treatment sector the number of measurements provided is extremely limited.
    - For the use as catalysts only six measurements with a high variability are available.
- The air monitoring data present a high variability for most of the activities:
    - Difference between median and the RWC is in the range of two to five times but higher than ten times for some tasks (e.g. packaging activities).
    - This high variability may be explained by the fact that the database is composed of data from different workplaces and compiled over a number of years.
    - It nevertheless reflects a high variability in operating conditions and risk management measures of the different workplaces.

For some of the exposure scenarios, for which specific monitoring data were not available, analogous data from other cobalt compounds and or activities have been used to estimate exposure (Cobalt REACH Consortium Ltd., 2018). Additionally, a number of exposure values are derived from modelling (MEASE (1.02.01)).

All exposure data presented in the registration dossiers correspond to the inhalable fraction.

An overview of exposure values as considered representative by the Dossier Submitter for each sector of use is shown in the table below. The values are compiled from the exposure scenarios of the registration dossiers.

Table 2: Exposure data (inhalable fraction) from the registration dossiers for the different sectors of manufacture and use (Cobalt REACH Consortium Ltd., 2018)

Sector / use / Activity	**Air concentration [a] µg Co/m³ (Median-RWC)**	**Exposure level [b] µg Co/m³ (RWC 8h TWA)**
Manufacture	54-808	8
Manufacture of chemicals	31-206	10
Manufacture of batteries	16-153	1
Manufacture of catalysts	12-21[c]	3
Manufacture of pigments and dyes	4-29	3
Use as catalysts	0.8-3[c]	3
Use in surface treatment		
- Formulation	2-4[c]	0.7 4

Sector / use / Activity	Air concentration [a] µg Co/m³ (Median-RWC)	Exposure level [b] µg Co/m³ (RWC 8h TWA)
- Passivation - Plating	2-4[c] 9-14[c]	7
Use in biotechnology		
- Biogas production - Fermentation and biotech processes - Animal feed	- 1 -	5[d] 0.3 2[d]
Bespoke uses		
- Humidity indicators - Water treatment chemicals - Laboratory reference standards	0.2[c] 19-168 1	0.1 17 0.3

a. Air monitoring measurements based on personal samplers (except where otherwise stated). The Reasonable Worst Case (RWC) is based on the 90th percentile unless otherwise stated. The values shown correspond to the activities within the sector showing the highest exposure levels in the exposure scenarios, excluding cleaning and maintenance. For intermediate uses, only activities where the cobalt salts are present are considered, i.e. before they are transformed into another substances.
b. Exposure levels based on RWC air concentration, taking the use of RPE (if applicable) and the duration of the activity (but not the frequency of activities per year) into account.
c. RWC based on the 95th percentile or the maximum value.
d. Modelled value (MEASE (1.02.01))

In general terms, it can be said that exposure levels (RWC 8h TWA) range from 1 to 10 µg Co/m³ for the majority of the uses of the cobalt salts:

- The manufacture of the cobalt salts and the manufacture of chemicals present exposure values in the range of 8 to 10 µg Co/m³.
- The formulation of water treatment chemicals shows higher values of 17 µg Co/m³,
- Fermentation and biotechnology processes and the manufacture of humidity indicators show levels of exposure well below 1 µg Co/m³.
- For the surface treatment sector, exposure values range from
    - 0.7 to 4 µg Co/m³ for formulation and passivation,
    - up to 7 µg Co/m³ for plating operations.

The scarce data on exposure related to similar activities gathered from the literature and other sources (see Table 3) do not contradict the values presented by the registrants.

Table 3: Exposure data from independent sources

Sector / use / Activity	Source	Exposure level µg Co/m³
Manufacture of cobalt sulphate and cobalt carbonate (among other cobalt compounds)	Sauni et al, 2014, epidemiology study in a cobalt manufacturing plant in Finland	20
Manufacture of cobalt metal		60
Compilation of cobalt exposure data from 2007 to 2017	France	
- Surface treatment activities - Feed grade materials		Median: 2, RWC: 75.5 Median: 1 RWC: 32.1
Passivation	Slovakia	below 4

The Dossier Submitter considers that the exposure levels reported in the registration dossiers can be used for risk assessment for all uses as presented in Table 2, in spite of the uncertainties mentioned above.

Especially relevant activities

The Dossier Submitter identifies a limited number of activities (see Appendix 3 of the Background Document where all the different tasks are described for each of the sectors of use, together with the exposure values and the operational conditions) that seem to have the potential of highest exposure:

- Tasks where the five cobalt salts are used in solid form (mainly as powder), e.g. loading, unloading, packaging, etc.
- Hot metallurgical process where the high temperatures increase the potential to generate airborne particles (e.g. calcination – heating to high temperatures in air or oxygen. Calcination is also used to mean a thermal treatment process in the absence or limited supply of air or oxygen applied to ores and other solid materials to bring about a thermal decomposition.)

These activities result in air concentration values of 200 µg Co/m^3 (RWC). On the other hand, the use of cobalt salts in aqueous solutions result in significantly lower inhalation exposure, ranging from around 0.5 to 5 µg Co/m^3. Electroplating, involving the use of electrical currents, produces air concentration levels in the range of 14 µg Co/m^3 while passivation (without electrical current) results in air concentration levels of 1 µg Co/m^3.

Combined exposure is expected – by the Dossier Submitter – to be higher for workers involved in several daily activities resulting in exposure to the cobalt salts.

Dermal exposure

No data on dermal exposure were available to the Dossier Submitter. The registration dossiers assess dermal exposure in a qualitative way and require the use of gloves and protective equipment to prevent potential dermal exposure. Good occupational hygiene practices are also recommended to prevent potential oral exposure to workers. Quantitative data regarding dermal exposure to the cobalt salts have been found neither in literature nor from other sources.

Due to the lack of data, the Dossier Submitter does not consider it feasible to make any qualitative or quantitative assessment of the dermal exposure arising from the manufacture and use of the cobalt salts.

RAC conclusions:

The data presented by the Dossier Submitter about **tonnages** are extracted from information provided by the Cobalt Institute in the call for evidence for the preparation of the restriction dossier and seem rather outdated. The use of cobalt salts is predicted to increase in the coming years. Therefore, the available data adds an additional uncertainty to RAC's assessment (see below in chapter "Uncertainties in the risk characterisation").

Some of the uses mentioned in Table 1 (e.g. use in fertilisers) seem not to take place in the EU at present but are "traditionally" linked to the five cobalt salts and were therefore included in the initial request by the Commission.

In some sectors of activity, cobalt salts are used in forms with lower exposure potential (e.g. use of coated granules in animal feed, manufacture of catalysts as cakes or pellets). It is, however, difficult to take any such reduced exposure potential into account for risk assessment, as the effect of exposure reduction potential cannot be quantified.

From an exposure assessment and substance properties point of view it is an unrealistic

assumption to use the inhalable fraction as the full respirable fraction as proposed by the Dossier Submitter. The Dossier Submitter's approach is further discussed in the hazard characterisation section. RAC concluded that a ratio of two (50% respirable dust) is still a reasonable worst case for the ratio of the respirable to the inhalable dust fraction. RAC agreed to take forward different values (50% and 100% fraction of respirable dust) for risk assessment in order to simplify comparisons.

The available data set for inhalation exposure has a number of significant limitations, which introduces a substantial level of uncertainty. It is therefore critical for RAC's risk assessment to identify conservative exposure levels. Appendix 3 of the Background Document presents a complete picture of all relevant sectors and uses of cobalt salts and activities performed with cobalt salts as described in the registration dossiers. In Appendix 3 for each activity, the relevant exposure level is described.

The values given in Table 2 represent 8h time weighted average (TWA) exposure levels based on the RWC air concentration, taking the use of RPE (if applicable) and the duration of the activity (but not the frequency of activities per year) into account. It is to be noted that these values are estimated taking into account the activity with the highest exposure level for each sector of use and do not consider the potential cumulative exposure resulting from different activities performed on the same shift by the same worker.

These values are associated with uncertainties (as described below). However, these levels of exposure have been supported in principal by different contributions during the consultation.

As the use of cobalt salts does not take place on a continuous basis in most sectors, the Dossier Submitter has considered the frequency and duration of each task, as presented in the exposure scenarios from the registration dossiers, for the calculation of the excess cancer risk values for each sector of use. This has a significant impact on the time-weighted exposure levels resulting from different tasks. It is unclear if the frequency and duration considerations are representative for the tasks in question, as the data on frequency and duration of the activities – as reported by industry – are based on a very limited number of companies.

It was not possible to trace all the calculations of the Dossier Submitter and the Registrants for the derivation of the exposure levels. With the additional data as provided by the Dossier Submitter it was possible to identify discrepancies between the 8h TWA RWC values for each sector of use as presented in Table 2 (equates to Table 4 in the Background Document) and those resulting from the combined annual exposure used for risk assessment (see Table 4). The 8h TWA RWC from Table 2 refer to the activity with the highest exposure level as 8h TWA for each sector of use. The exposure levels used for risk characterisation (Table 4) result from the highest annual combined exposure for workers taking the frequency and duration of each activity into account.

For some uses / activities the Dossier Submitter used modelled or analogous data. This use of modelling or analogous data is not justified in the dossier nor is the modelling transparent (input parameters, model outputs). Justification and reasoning for this "read across" and modelling are not available in the restriction proposal. During the consultation, the Cobalt REACH Consortium Ltd. and Cobalt Institute provided some justifications regarding the use of analogous data. The approach taken by industry is now transparently described and understandable. The clarifications provided in the consultation reduces the uncertainty of the analogous data to some extent. The modelled data are still uncertain.

Despite the limitations described above, RAC concludes that the level of exposure as presented in **Table 4** is in a reasonable order of magnitude given that information provided during the consultation by different contributors in principal confirms the order of magnitude of the exposure levels.

Table 4: Exposure data (inhalable fraction) used by RAC

Sector / use / Activity	**Exposure levels used by the Dossier Submitter for Excess Lifetime Risk calculation (µg Co / m³)**
Manufacture	9.5
Manufacture of chemicals	5.0
Manufacture of batteries	3.3
Manufacture of catalysts	0.9
Manufacture of pigments and dyes	5.0
Use as catalysts	3.1
Use in surface treatment	
- Formulation - Passivation - Plating	0.28 4.3 11.4
Use in biotechnology	
- Formulation and industrial use of mixtures in biogas production - Professional use in biogas production - Fermentation and biotech processes - Animal feed	2.6 0.015 0.18 0.22
Bespoke uses	
- Humidity indicators - Water treatment chemicals - Laboratory reference standards	0.061 3.3 0.13

Within the uses, only a limited number of tasks / activities seem to contribute in a relevant manner to the exposure. However, it was not possible to identify a pattern. Obviously it is possible to identify for each of the sectors the task / activity that contributes the largest fraction to the overall exposure. It was a relevant exercise to identify those activities with high inhalation exposure and try to address these by fit-for-purpose risk management measures and operational conditions. The result of this exercise, however, is that the same or similar task has not the same importance for another sector of use. Therefore, it was not possible for RAC to identify a limited number of activities that could be addressed individually.

Dermal exposure (and potential oral exposure) is only briefly discussed by the Dossier Submitter. This could be accepted by RAC due to the limited scope of the restriction and the risk that shall be addressed by the restriction. The lacking information on dermal exposure adds an additional uncertainty to RAC's assessment (see below in chapter "Uncertainties in the risk characterisation") because a full risk characterisation would include also dermal aspects. This is especially relevant for these five cobalt salts as they are skin sensitisers.

Key elements underpinning the RAC conclusions:

Regarding the **ratio of respirable to inhalable dust,** Appendix 2 of the Background

Document and contributions in the consultation include relevant information:

Industry assessment (resulting in a 10% respirable fraction):

- This assessment is only based on two of the three workplaces that were monitored by Institute of Occupational Medicine → only 11 data points
- Also in that study a relevant number of measurements show a ratio that is higher than 10 % respirable fraction, i.e. up to 23%
- Respirable particles can also be bigger than considered in this assessment

Therefore, a 10% respirable fraction is not conservative.

The study by Okomato at al.(1998):

- is based on > 1 600 data points
- Shows big variation in the data depending on the type of work and, probably, also on the work conditions.
- 20% - 50% respirable fraction seems plausible

Therefore, a 50 % respirable fraction would be an appropriately conservative assumption.

During the consultation, it was addressed that the preventive approach (100% respirable fraction) of the Dossier Submitter is unrealistic. The Cobalt REACH Consortium Ltd. and the Cobalt Institute submitted additional information on particle size distribution of cobalt containing alloys composed primarily of tungsten carbide and cobalt, which are used in cutting tools. However, this publication (Stefaniak et al. (2009)) seems of limited relevance for the five cobalt salts in question here.

Overall, RAC considers 10% as the respirable fraction as unrealistic and concludes therefore that 50% respirable fraction is a more conservative assumption, based on the Okamata study.

The dataset for inhalation exposure shows a number of deficiencies that add to the overall uncertainty of the risk assessment that needs to be quantified (see below in chapter “Uncertainties in the risk characterisation”):

- It is considered a major deficiency by RAC that the registrant’s exposure data could not be validated by independent sources.
    - The Dossier Submitter provided almost only data from the registration dossiers.
    - The scarce data on exposure related to similar activities gathered from the literature and other sources (see Table 3) do not contradict the values presented in the registration dossiers. However, the presented data from independent sources are by no standards sufficient to validate the inhalation exposure situation at European workplaces.
- After some clarification by the Dossier Submitter, the RWC derivation is also not entirely transparent and obviously differs for different sectors:
    - Registrants used the 90th percentile value to define the RWC for datasets with at least six measurements.
    - Either the 95th percentile or the maximum were used as RWC for datasets with less than six measurements

- The use of cobalt salts does not take place on a continuous basis (i.e. not every day, not the full shift) in most sectors and this has a significant impact on the time weighted exposure levels resulting from different tasks.
- The registration dossiers identify the frequency and duration of each exposure scenario for which exposure levels are calculated. Registrants and Dossier Submitter consider these parameters as representative of the activities taking place in each sector.
- Additional data regarding inhalation exposure was provided during the consultation. This data principally confirmed the order of magnitude of inhalation exposure of workers.
    - The Cobalt REACH Consortium Ltd. and the Cobalt Institute submitted additional data, e.g. from the surface treatment sector with a significant number of data points (i.e. more than 20 measurements).
    - Other respondents to the consultation provided qualitative information claiming that monitoring in the past showed that national OELs were complied with.

Despite the limitations in the dataset for inhalation exposure, RAC considers the level of exposure as presented in Table 4 to be in a reasonable order of magnitude and will use these values as the basis for risk assessment.

Due to the large number of scenarios and uses it is considered reasonable to only evaluate one sample use here in some more detail with regard to frequency and duration of the tasks.

For the manufacture of the cobalt salts the relevant tasks are presented in Figure 1 and show:

- The duration of the task per shift varies from approx. 15 minutes per shift to almost five hours.
- The frequency of the task (in how many shifts per year is the task in question performed) varies from 20 to 240 (everyday).
- The reasonable worst case (RWC, air concentration data) in µg Co/m³ varies from five to more than 800. The RWC as an 8h TWA (incl. adjustment for RPE and exposure duration) varies from 0.03 to 7.7.

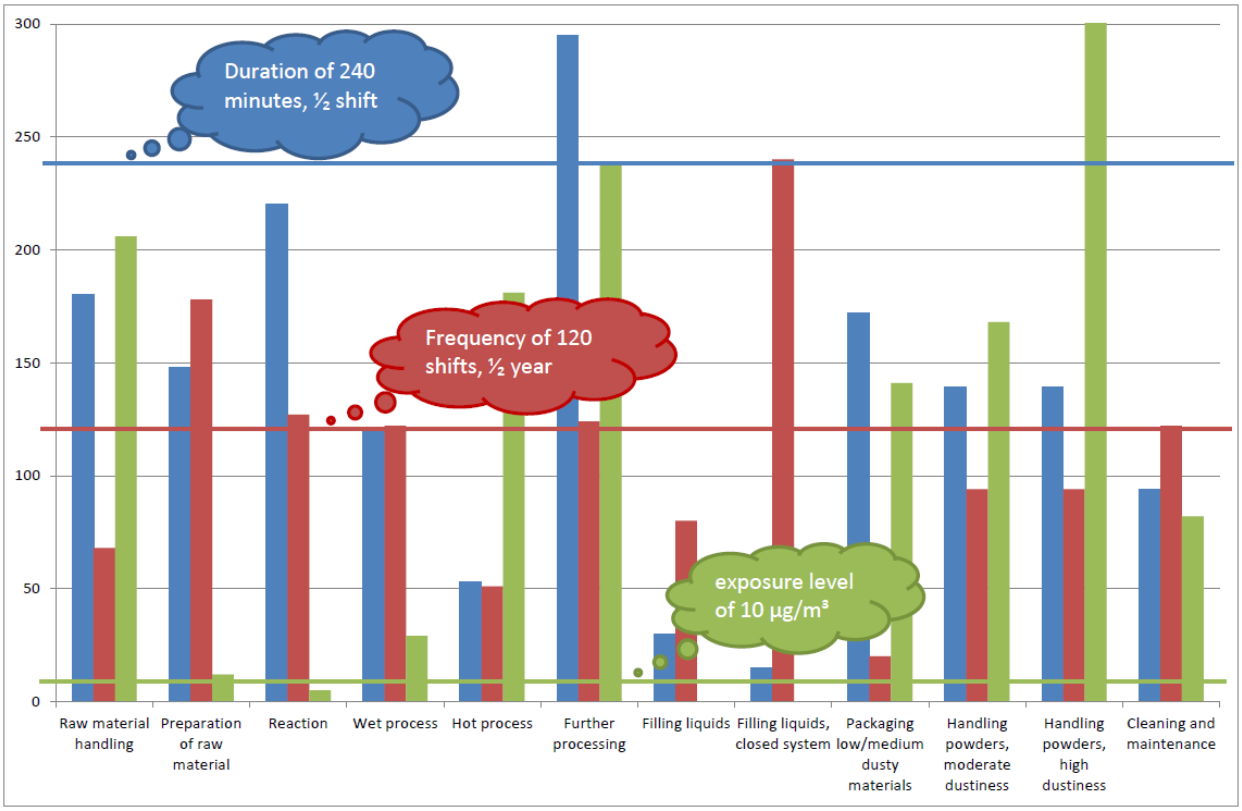

Figure 1: Manufacture of the cobalt salts

Duration (min) of the task per shift

Frequency of the task (no of shifts per year)

RWC (µg Co/m³) (Air concentration data)

The picture is not identical, but sufficiently similar, for the other uses (manufacture of chemicals, manufacture of batteries, manufacture of catalysts, manufacture of pigments and dyes, use as catalysts, use in surface treatment, use in biotechnology and the bespoke uses) to reach the conclusion that an adjustment for duration and frequency is warranted to be done on a task by task basis. The data on duration and frequency of the single tasks were made available to RAC by the Dossier Submitter and are documented in Appendix 3 of the Background Document.

As described above, it is not possible to identify a number of tasks / activities with a higher potential for exposure and that could be restricted individually.

Characterisation of risks

Summary of proposal:

Applying the RAC (2016) dose-response curve for the carcinogenicity of cobalt and the exposure assessment presented in the previous chapter, the Dossier Submitter calculated individual excess lifetime cancer risk levels significantly above 10^{-5} for all sectors assessed.

The major contributors to the cancer risk levels were those tasks with the highest potential for inhalation exposure, e.g. handling of cobalt salts in solid, dusty form and activities where high energy is applied (temperature and/or electrical currents), such as electroplating. This is the case in those sectors with the highest individual excess lifetime cancer risk levels, i.e. manufacture and electroplating where excess cancer risk levels are estimated at or above 10^{-2}.

In other sectors, excess cancer risk levels are above 10^{-3} (e.g. manufacture of chemicals, manufacture of batteries, etc.) and 10^{-4} (e.g. manufacture of catalysts, formulation of feed grade materials, etc.). Based on these findings, the Dossier Submitter identified that cancer risks to workers are currently not adequately controlled and that these risks need to be addressed at the Union level.

The Dossier Submitter proposed that individual excess cancer risks should be reduced to 10^{-5} or below to ensure a high level of protection of workers from the risk of developing cancer due to exposure to the cobalt salts. Based on linear extrapolation, individual excess cancer risk levels below 10^{-5} result from a lifetime exposure to cobalt below 0.01 µg Co/m^3, i.e. this value was proposed to be applied as a reference exposure value (REV) for the occupational exposure to cobalt.

Even though it was recognised that the linear extrapolation is likely to overestimate the individual excess life-time cancer risk, this was not taken into account in the proposal. Since there is no consensus on the acceptable cancer risk level for occupational exposure in the EU, the selection of a cancer risk level of 10^{-5} was based on REACH guidance (Chapter R8-Appendix 14, page 140), which states that "*the decision point for 'acceptable' lifetime (i.e., a working life of 40 years) cancer risk levels used for workers are generally around 10^{-5} but higher or lower levels have been considered to be tolerable under certain circumstances.*"

RAC conclusions:

As discussed above, the Dossier Submitter's approach to use linear extrapolation for the risk assessment of cobalt salts, combined with the assumption that the risk of systemic and upper respiratory tract cancers is similar to that of lung cancer, is considered over-conservative and is hard to justify as a reasonable worst case (RWC) scenario. Therefore, RAC re-calculated the excess lifetime risks for different uses using 50% as a conservative estimate of the proportion of respirable dust and a breakpoint approach as described by the German Ausschuss für Gefahrstoffe - AGS (TRGS 910, 2014). This approach is considered to better reflect the current scientific understanding on the lung carcinogenicity of cobalt and to provide a more realistic but still conservative estimate on the risks. It assumes that the risk of cancer is reduced by a factor of 10 at the breakpoint exposure level identified based on toxicological data. In the case of cobalt, the breakpoint level is 0.5 µg Co/m^3 (as respirable fraction).

The risk at doses above the breakpoint can be calculated using the formula:

1.0576 x exposure concentration (as mg Co/m^3, respirable fraction) - 0.0004763

The risk below the breakpoint follows the formula:

0.105 x exposure concentration (as mg Co/m^3).

Using this approach, the following excess lifetime risks can be calculated for the different RO1 options proposed by the Dossier Submitter:

- RO1a 10 µg Co/m^3 (as inhalable fraction), meaning 5 µg Co/m^3 as respirable fraction corresponds an excess lifetime risk of 4.8 x 10^{-3}
- RO1b 1 µg Co/m^3 (as inhalable fraction), meaning 0.5 µg Co/m^3 as respirable fraction corresponds an excess lifetime risk of 5.25 x 10^{-5}

- RO1c 0.1 µg Co/m^3 (as inhalable fraction), meaning 0.05 µg Co/m^3 as respirable fraction corresponds an excess lifetime risk of 5.25 x 10^{-6}
- RO1d 0.01 µg Co/m^3 (as inhalable fraction), meaning 0.005 µg Co/m^3 as respirable fraction corresponds an excess lifetime risk of 5.25 x 10^{-7}

It is not possible to identify a dose-response or set a limit values for the respiratory sensitisation caused by cobalt. However, based on the available (although limited) data it can be anticipated that at the level of 1 µg Co/m^3 cases of asthma are unlikely.

According to RAC's analysis (see Table 4), there are several activities that can result in exposures above the breakpoint level of 0.5 µg Co/m^3 (corresponding to 1 µg Co/m^3 inhalable fraction). These include e.g. manufacturing of cobalt salts, chemicals, pigments and batteries and the use of cobalt salts as catalysts in surface treatment. Using the approach above, these activities result in excess lifetime cancer risks that for some are even > 10^{-3} (see further table 5).

With the exception of catalyst manufacturing, mainly lower volume activities (e.g. the use in biogas production, in fermentation processes and feed grade materials) result in exposure levels below the estimated breakpoint of 0.5 µg Co/m^3. Assuming that at the breakpoint of 0.5 µg Co/m^3 the risk is lowered by a factor of 10 the estimated lifetime cancer risk at these tasks varies from <10^{-6} to approx. 5 x 10^{-5} (see table 5 below).

Given that there are several uses/activities that show cancer risks even >10^{-3}, RAC concluded that there are risks from exposure to cobalt that are not adequately controlled.

It should be noted that when the breakpoint level of 1 µg Co/m³ (inhalable fraction) and 0.5 µg Co/m³ (respirable fraction) is applied as an 8 h TWA level (instead of as a frequency adjusted level), it is likely to result in lower annual average exposures and therefore lower cancer risk in those low frequency scenarios which have higher short-term exposures.

Key elements underpinning the RAC conclusions:

The excess lifetime risks calculations made by RAC (in addition to those presented by the Dossier Submitter) are presented in Table 5. The RAC approach includes the proportion of 50% for respirable/inhalable dust, and the use of breakpoint at 0.5 µg Co/m^3 for the carcinogenicity of Co (see below).

Table 5: Risks calculated using Dossier Submitter's approach and RAC approach. Colours: orange risk $<10^{-5}$, violet risk $<10^{-4}$.

Sector / use	Exposure levels used for ELR calculation (µg / m³)	ELR estimated by Dossier Submitter with 100 % respirable fraction and linear dose-response	ELR estimated by RAC with 50 % respirable fraction and non-linear DR with a breakpoint at 0.5 µg / m³ *
Manufacture of the cobalt salts	9.5	1.0E-02	4.6E-03
Manufacture of chemicals	5.0	5.3E-03	2.2E-03
Manufacture of batteries	3.3	3.5E-03	1.3E-03
Manufacture of catalysts	0.9	9.4E-04	4.7E-05
Manufacture of pigments and dyes	5.0	5.2E-03	2.1E-03
Use as catalyst	3.1	3.3E-03	1.2E-03
Use in surface treatment			
- Formulation of surface treatment solutions	0.28	2.9E-04	1.5E-05
- Passivation or anti-corrosion treatment processes	4.3	4.5E-03	1.8E-03
- Metal or metal alloy plating	11.4	1.2E-02	5.6E-03
Use in biotechnology			
- Formulation and industrial use of mixtures in biogas production	2.6	2.7E-03	8.8E-04
- Professional use in biogas production	0.015	1.6E-05	8.0E-07
- Use in fermentation processes, in biotech and scientific research and standard analysis	0.18	1.9E-04	9.5E-06
- Formulation and use in feed grade materials	0.22	2.3E-04	1.2E-05
Bespoke uses			
- Use in humidity indicator cards, plugs and/or bags with printed spots	0.06	6.4E-05	3.2E-05
- Formulation of water treatment chemicals, oxygen scavengers, corrosion inhibitors	3.3	3.5E-03	1.3E-03
- Use of water treatment chemicals, oxygen scavengers, corrosion inhibitors	0.13	1.4E-04	7.0E-06

*Breakpoint which is assumed to reduce the risk with a factor of 10.

The Dossier Submitter has set a reference exposure value (REV) for cobalt salts corresponding to a cancer risk level of 1 x 10^{-5} derived using a linear approach. RAC recognises that the risk level of 1 x 10^{-5} is mentioned in REACH guidance as an example with a statement that lower or higher risk levels can be justified under certain circumstances. However, it should be noted that there is no political consensus on the acceptable risk level for carcinogenicity in the EU. In the case of authorisations, long review periods based on socio-economic considerations have been proposed by SEAC regardless of risk levels around 10^{-3}, or even higher, for example in some chromium(VI) and arsenic trioxide authorisations. As discussed in ECHA R.8 Guidance, Appendix 14, tolerable/acceptable cancer risk levels for workers usually vary between 10^{-3} – 10^{-5} in different (often outdated) Risk Assessment frameworks/countries. In addition, even greater risks have been accepted due to socio-economic reasons; an example of which is the binding occupational exposure level (BOELV, 2017) for Cr(VI) of 5 µg/m^3, which represents a calculated risk of 2*10^{-2} over 40 years occupational exposure. Transitional measures for Cr (VI) include, among others, an occupational limit value of 0.010 µg/m^3 until 2025 corresponding to an excess cancer risk level of 2*10^{-2}.

Compared to hexavalent chromium, which is a direct DNA-acting genotoxic carcinogen, the main mechanisms of cobalt genotoxicity and carcinogenicity are likely to include a breakpoint. Thus, the risk of lung cancer is likely to be significantly lowered compared to the risks estimated on the basis of linear extrapolation at exposure levels below this breakpoint. RAC has estimated that this breakpoint in the dose-response curve of cobalt lays around 0.5 µg Co/m^3 (respirable fraction). Below the breakpoint, the risk is assumed to be one order of magnitude lower. This is a default assumption used by the German AGS when setting tolerable and acceptable risk levels for this type of carcinogen. Using this approach, and the formulas given in the previous section, the cancer risks at exposure levels of 5 µg Co/m^3, 1 µg Co/m^3, 0.5 µg Co/m^3 or 0.1 µg Co/m^3 (as respirable fraction) can be calculated at 4.8*10^{-3}, 6*10^{-4}, 5.25*10^{-5}, 1*10^{-5}, respectively. On the basis of human data, it was possible for RAC to estimate a limit value of 1 µg Co/m^3 for the inhalable fraction in order to protect from non-cancer respiratory effects (effects on lung function). The respirable fraction represents usually ≤50% of inhalable dust meaning that at this level the levels of respirable dust are usually below 0.5 µg Co/m^3.

As can be seen from Table 5, despite these adjustments to the risk calculations there are still several uses which show risks >10^{-3}, meaning that risks from cobalt exposure have been identified that are not adequately controlled.

The REV proposed by the Dossier Submitter is a frequency and duration-adjusted limit value. As discussed in the hazard section, if the breakpoint level of 1 µg Co/m^3 (inhalable fraction) and 0.5 µg Co/m^3 (respirable fraction) are applied as limit values, they should be used as an 8 h TWA level. These exposure levels do not necessarily result in significant increases above the normal background reference levels when cobalt exposure is biomonitored using urinary cobalt as a marker of systemic exposure (see Appendix 7 of the Background Document on biomonitoring). Biomonitoring can, however, be used to give indirect information on possible dermal exposure (including hand-to-mouth exposure). Monitoring and control of skin exposure is important because of the skin sensitising properties of cobalt.

Uncertainties in the risk characterisation

The main assumptions and uncertainties of the risk characterisation and their potential

impacts are presented in Table 6 below.

In summary, the Dossier Submitter estimates that the potential impact of the uncertainties in the assessment are from moderate to high and may result both in an overestimation or underestimation of the net benefits of the restriction. Using the modified approach proposed by RAC, some overestimations in the risk characterisation are avoided.

Table 6: Assumptions and uncertainties

Assumptions / Uncertainties	Description / Justification	Reference to Background Document	Impacts the following outcomes	Potential over- / under-estimation of net benefits of restriction	Potential magnitude of impact
Non-threshold effect	The suggested cancer mechanisms may have a threshold even if the current data does not allow identification of this.	Section 1.2.4.2 Section B.4.4.3	Risk estimates Baseline cancer cases Benefits of restriction	Over	Originally high. Applying a breakpoint approach, the magnitude of over-estimation is lowered to low.
Assumed linearity for low exposure levels	The dose response relationship was derived by linear extrapolation, which may lead to an overestimation of risks, especially at very low exposure levels.	Section 1.2.4.2 Section B.4.5	Risk estimates Baseline cancer cases Benefits of restriction	Over	Originally high. Applying a breakpoint approach and risk reduction by a factor of 10 at the levels below the breakpoint, the magnitude of over-estimation is lowered.
Ratio inhalable to respirable fraction	The ratio inhalable to respirable fraction is estimated at 2 based on the Okamoto's study (1998).	Appendix 2	Baseline cancer cases Benefits of restriction	Over	Medium
Cancer risk from non-respirable fraction	According to RAC (ECHA, 2016), the non-respirable fraction should be considered as carcinogenic. The dose-response relationship for the non-respirable fraction was not derived since not enough data were available for this metric. RAC did not agree with Dossier submitter to apply the	Section 1.2.4.2 Section B.4.5	Risk estimates Baseline cancer cases Benefits of restriction	Under	Low

Assumptions / Uncertainties	Description / Justification	Reference to Background Document	Impacts the following outcomes	Potential over- / under-estimation of net benefits of restriction	Potential magnitude of impact
	dose-response for respirable fraction to characterise all cancer effects (local and systemic) resulting from exposure to the cobalt salts because of the potency difference evident from animal data				
Skin and respiratory sensitisation, asthma effect	The focus of the restriction is on the carcinogenicity of the cobalt salts. The quantification of impacts do not consider other health effects.	Section 1.2.4.1	Baseline impacts Risk reduction capacity Benefits of restriction	Under	Low
Reproductive toxicity	The focus of the restriction is on the carcinogenicity of the cobalt salts. The quantification of impacts do not consider other health effects.	Section 1.2.4.1	Baseline impacts Risk reduction capacity Benefits of restriction	Under	Low
Exposure values	The number of measurements vary between industrial sectors. In some sectors only one measurement is available for some activities and for some activities the exposure is based on modelling. Very few data are available in the literature to validate the data presented by industry.	Section 1.2.5.2 Appendix 3	Risk estimates Baseline cancer cases Risk reduction capacity Benefits of restriction	Both	High
Dermal exposure	Dermal exposure is only discussed briefly	Section 1.2.5.2	Dermal exposure might lead to skin sensitisation and allergies	Under	Low
Analytical methods	The measurement procedures presently used for the monitoring of cobalt concentration in air do not allow detecting values below 1µg Co/m^3. Exposure levels may be lower than those reported for some activities.	Section 2.6.3	Risk estimates Baseline cancer cases	Over	Low

Assumptions / Uncertainties	Description / Justification	Reference to Background Document	Impacts the following outcomes	Potential over- / under-estimation of net benefits of restriction	Potential magnitude of impact
Concomitant exposure to other cobalt compounds	The measurements are from workplaces where the five cobalt salts and possibly other cobalt substances are manufactured and used. The measured cobalt levels may report exposure to a variety of cobalt compounds and not only to cobalt salts.	Section 1.5.2. Appendix 3	Risk estimates Baseline cancer cases Risk reduction capacity Benefits of restriction	Over	Low
Typical and reasonable worst case exposure level and risk reduction capacity	The estimation of the baseline cancer cases and risk reduction capacity is based on improvements from the reasonable worst case exposure levels (for 10% of the companies) and typical level (for the rest of the affected companies). This affects also the estimated costs under RO1, as the cost for each industrial sector is derived from the effectiveness needed to reach the reference exposure value. It is not clear if this is representative for the different risk levels in the affected companies.	Section 1.4 Section 2.5	Baseline cancer cases Risk reduction capacity Benefits of restriction	Both	Low
Duration and frequency of the activities	Information is from limited sources and cannot be verified.	Appendix 3	Risk estimates Baseline cancer cases Risk reduction capacity Benefits of restriction	Both	High
Combined exposure	The estimation of the individual worker cancer risks is based on the combined exposure resulting from the worst case combination of tasks a worker can in theory conduct.	Section B.10	Risk estimates Baseline cancer cases Risk reduction capacity Benefits of restriction	Over	Medium
Number of exposed workers per sector	Estimated number of exposed workers is provided by the industry. It is based on limited data and cannot be	Section 1.4	Baseline cancer cases Risk reduction capacity	Under	Medium to High

Assumptions / Uncertainties	Description / Justification	Reference to Background Document	Impacts the following outcomes	Potential over- / under-estimation of net benefits of restriction	Potential magnitude of impact
	verified. However, the use of Co is expected to grow, which can lead to higher number of affected worker per sector.		Benefits of restriction		
Number of sites per sector	Estimated number of companies per sector is provided by the industry. It is based on limited data and cannot be verified. However, the use of Co is expected to grow, which can lead to higher number of affected sites in some sectors as new sites might be opened.	Section 1.4	Risk reduction capacity Benefits of restriction Cost of restriction	Both, depending on OCs/RMMs in the new sites.	Medium to high
Regrettable substitution	As this restriction proposal covers five specific Cobalt salts some users might substitute these five salts with other Cobalt compounds.	---	Risk reduction capacity	Over	unknown

At the request of the RAC Rapporteurs, the Dossier Submitter has performed a sensitivity analysis for those variables with the highest impact on the risk assessment. Low and high values were selected for each variable based on the Dossier Submitter's expert judgment. The results of the analysis are shown in Table 7. In general terms, it is considered that underestimation or overestimation of the risks may be up to one order of magnitude for some parameters.

Table 7: Sensitivity analysis on parameters affecting individual risk levels

Variable	Present Values	Low value for sensitivity analysis	High value for sensitivity analysis	Impact	Low range	High range
Mode of action	Non-threshold	Threshold at 0.5 µg/m³	Non-threshold	Individual risk levels	Safe use in seven sectors of use	ELR from 10^{-5} to 10^{-2}
Dose-response	Linear; 1.05 x 10^{-3}	Non-linear below 0.5 µg/m³: 1.05 x 10^{-4}	Linear; 1.05 x 10^{-3}	Individual risk levels	For those sectors with ELR ≤ 5*10^{-4}, ELR is divided by 10 ELR from 10^{-6} to 10^{-2}	ELR from 10^{-5} to 10^{-2}
Ratio of inhalable fraction to respirable fraction	2	10	1	Individual risk level	ELR divided by 10 * ELR from 10^{-6} to 10^{-3}	ELR from 10^{-5} to 10^{-2}

Variable	Present Values	Low value for sensitivity analysis	High value for sensitivity analysis	Impact	Low range	High range
Cancer risk from non-respirable fraction	1.05 x 10^{-3}	Non-carcinogenic	1.05 x 10^{-3}	Individual risk level		
Exposure values	In the range of 1 to 10 µgCo/m³	0.5 to 5 µgCo/m³	10 to 100 µgCo/m³	Individual risk levels	ELR divided by 2 ELR from 10^{-6} to 10^{-3}	ELR x 10 ELR from 10^{-4} to 10^{-1}**
Duration and frequency of activities	Depending on the sector	Present values	Daily activity, i.e. 240 days/year	Individual risk levels	ELR from 10^{-5} to 10^{-2}	ELR x 2 up to x 10 depending on the sector. ELR from 10^{-5} to 10^{-2}

* Assuming the non-respirable fraction is non-carcinogenic
** RAC notes that risk of 10^{-1} in manufacturing and electroplating is not in accordance with the available human evidence, which have not shown increased risks. An excess risk of 10^{-1} is so high that it should have been seen even in smaller cohorts.

Although the combination of several variables may result in a higher order of variation, it may also have a counterbalancing effect and decrease the overall range of uncertainty. However due to the number of different combinations that may be possible, and the complexities inherent to the variation of a number of parameters, this analysis has not been attempted.

In conclusion, there is considerable uncertainty in those aspects affecting the exposure assessment part, i.e. exposure assessment, substance properties (e.g. particle size distribution), and e.g. organisation of workplaces. However, as there is information mainly confirming the order of magnitude of the exposure, RAC considers the risk characterisation reasonably certain and concludes that for cobalt there is a need to decrease exposure in order to adequately control the (cancer) risks.

Evidence if the risk management measures and operational conditions implemented and recommended by the manufactures and/or importers are not sufficient to control the risk

Summary of proposal:

In registration dossiers, industry has used a DNEL value of 40 µg Co/m³, and this has not been updated to take into account the RAC (2016) opinion on the carcinogenicity of cobalt salts. The available information does not suggest any trend in the implemented risk management measures, or in the exposed population that would have lowered the exposure, individual risk levels or the annual excess cancer cases.

The Dossiers Submitter derived a reference exposure value of 0.01 µg Co/m³ for the inhalable fraction of cobalt connected with an excess lifetime risks of 10^{-5}. This approach resulted in all relevant activities falling above the reference exposure value.

RAC identified a breakpoint of 0.5 µg/m³ (respiratory fraction) for the carcinogenicity of

cobalt. RAC notes that in several activities this exposure level of 0.5 µg/m³ is exceeded.

Both these approaches have in common that there are a relevant number of activities with exposure levels clearly above the respective reference/limit values. Rather surprisingly, this holds true even for a DNEL value of 40 µg Co/m³ as proposed in the registration dossiers.

RAC conclusions:

RAC agrees with the Dossier Submitter that based on the available exposure information, the risk management measures (RMMs) and operational conditions (OCs) implemented and recommended by the manufacturers and importers are not sufficient to control the risks. Additionally, according to the information provided in the registration dossiers and in the consultation there are a wide range and high diversity of exposure levels and RMMs and OCs implemented at workplaces even at those workplaces with similar activities but also between different industrial sectors.

Key elements underpinning the RAC conclusions:

RAC's conclusion is based on following arguments:

- In many sectors, estimated exposures are clearly above 0.5 µg Co/m³ (respirable fraction), representing a cancer risk of > 5.25 x 10^{-5}. In some sectors (manufacturing, surface treatment) exposures may be even higher than 10 µg Co/m³ (inhalable fraction, corresponding to 5 µg/m³ as respirable fraction) representing a cancer risk of > 4.8 x 10^{-3}.

- Based on some of the reported exposure values even the DNEL reported in the registration dossiers is exceeded for some uses.

- During the consultation, information was provided confirming the overall picture regarding exposure at workplaces. Exposure levels have not changed for some uses and the level of protection (RMMs/OCs) are the same as documented in the registration dossiers. In fact, contributions during the consultation confirmed the exposure levels as presented in the registration dossiers.

Evidence if the existing regulatory risk management instruments are not sufficient

Summary of proposal:

According to the Dossier Submitter, the cobalt salts are manufactured in a few but used in many (if not all) EU member states and pose a risk to the workers exposed that is not adequately controlled. At present, 15 EU member countries have implemented regulatory measures (OELs) to limit exposure of workers to cobalt (section B.9.1.2) but these vary between the countries regarding their level (5 µg/m³ in Germany to 500 µg/m³ in Latvia, all values given as 8h TWA limit values).

Using the RAC dose-response relationship from 2016, and estimating typical and reasonable worst case exposure, the Dossier Submitter estimated expected individual risk levels and annual cancer cases linked to the use of the cobalt salts per sector. According to the Dossier Submitter assessment, surface treatment, manufacture of cobalt salts, and manufacture of

other chemicals are the sectors with the highest exposure and risk. Highest individual excess cancer risks calculated for the manufacturing of cobalt salts and surface treatment sectors were in the order of magnitude of $1*10^{-2}$. In total, the current manufacture and use of the cobalt salts is estimated to cause excess cancer risk to approximately 35 000 workers and result therefore in approximately 40 cancer cases after lifetime exposure, i.e. one statistical cancer case per year.

Additionally, the volumes of the five cobalt salts used annually in the EEA is estimated to have doubled in the last 10 years and this increase is expected to continue in the future due to the increasing demand for rechargeable batteries in electric vehicles and biotechnology-health applications.

RAC conclusions:

RAC agrees with the Dossier Submitter that individual excess lifetime risks especially in some specific sectors of use exceed even a level of 1×10^{-3} and the information provided by industry in the consultation did not show any indication that the situation has changed. In addition, there is no cobalt-specific, EU wide regulatory measure (such as a binding OEL) implemented to limit the exposure to cobalt and the current OELs in Member States vary considerably. In conclusion, this means that the existing regulatory risk management instruments vary in the European Union and might lead to the above values for individual excess lifetime risks for lung cancer.

Key elements underpinning the RAC conclusions:

RAC's conclusion is based on following arguments:

- RAC agrees with the Dossier Submitter that individual excess lifetime risks especially in some specific sectors of use exceed a level of 1×10^{-3} (the level of 1×10^{-2} – also mentioned by the Dossier Submitter – is, according to RAC's evaluation, over conservative).

- There was no clear indication of the implementation of additional advanced RMMs or OCs by industry, e.g. during consultation.

There is no EU wide binding OEL for cobalt (or any other EU wide regulatory Co-specific risk management) and the current OELs in Member States vary.

JUSTIFICATION IF ACTION IS REQUIRED ON AN UNION WIDE BASIS

Justification for the opinion of SEAC and RAC

Summary of proposal:

The Dossier Submitter proposes to restrict the placing on the market, manufacture and use of five cobalt salts, where risks have been identified that are not adequately controlled. The substances are manufactured and used in a variety of sectors within the European Economic Area.

This includes the manufacture of chemicals, catalysts, battery production, surface treatment, fermentation processes, health applications, feed grade materials, biogas, etc. The substances are manufactured and used in many (if not all) EU member states. There are

currently around 30 000 tonnes of cobalt salts used in the European Union per year, the volumes placed on the EU market having doubled in the past ten years. The rise in demand is expected to continue in the near future due to increasing demand of rechargeable batteries and biotechnology-health applications. It is estimated that currently around 35 000 workers at around 20 000 industrial sites are exposed to the substances, for which the Dossier Submitter concludes that the risk they pose to workers is not adequately controlled and risk management is required at Union wide level.

At the request of the European Commission (EC), ECHA conducted an investigation on the uses of the cobalt salts in order to determine whether they pose a risk to human health which is not adequately controlled and should be addressed within the scope of an Annex XV restriction dossier. The report (2013) concluded that a significant potential for exposure to the cobalt salts could not be demonstrated for the uses covered by the study. However, this conclusion is based on a number of uncertainties, which could have a major impact on its outcome. Furthermore, several deficiencies in the registration dossiers were identified during the preparation of the report (for any details, please see the respective sections of the Annex XV restriction report and of this opinion respectively). Therefore, ECHA prepared a new report (2017) based on new data available which reveals excess cancer risk values in the range of 10^{-5} to 10^{-2} throughout the sectors concerned which lead to the Commission requesting ECHA to prepare the current restriction proposal.

The proposal applies to placing on the market, manufacture and use of the five cobalt salts as substances on their own or in mixtures in a concentration equal or above 0.01% by weight (i.e. the specific concentration limit for carcinogenicity 1B according to the harmonised classification and labelling of the cobalt salts) in industrial and professional applications. No consumer uses were identified by the Dossier Submitter and those are therefore out of the scope of this restriction proposal.

On the basis of the information summarised above, the Dossier Submitter concludes that a Union-wide regulatory measure is needed to ensure a harmonised high level of protection of human health. Furthermore, a Union-wide measure is regarded as preferable to varying regulatory standards and statutes in different EU member states and a unified regulation is said to minimise the potential of market distortion.

SEAC and RAC conclusions:

Based on the key principles of ensuring a consistent level of protection across the Union and of maintaining the free movement of goods within the Union, SEAC and RAC support the view that any necessary action to address risks associated with the use of five cobalt salts should be implemented in all Member States.

Key elements underpinning the SEAC and RAC conclusions:

RAC's view:

As stated above, the five cobalt salts under consideration are manufactured and used in many, if not all, EU member states. They are used within different sectors such as the manufacture of chemicals, batteries, catalysts, in the pigments and dyes production, in surface treatment processes, in the biotechnology (and health) sector, etc. and for different activities. The five substances are included in the candidate list under REACH due to their carcinogenic and repro-toxic properties and have also been prioritised for inclusion in the authorisation list (Annex

XIV). In addition, requirements relating to the European occupational health and safety legislation[16] apply, such as assessing and managing the risk of exposure to carcinogens or mutagens, reducing the use of relevant substances by replacing them with substances not dangerous or less dangerous, preventing worker exposure, using different technical measures such as closed technological systems, etc. Currently, 15 Member States have regulatory measures in place in order to limit the cobalt exposure to workers (only two Member States address specifically some of the five cobalt salts).

RAC confirms that risk management measures and operational conditions implemented and recommended by the manufacturers and importers throughout the Union are not sufficient to control the risks of the substances under consideration. RAC agrees with the Dossier Submitter that individual excess lifetime risks, especially in some specific sectors of use, exceed even a level of 1 x 10^{-3} and there was no indication of changes to these levels by industry during the consultation. RAC concludes that the existing European regulatory risk management instruments (e.g. current OELs in Member States) vary, which might lead to the above stated values for individual excess lifetime risks for lung cancer.

JUSTIFICATION WHETHER THE SUGGESTED RESTRICTION IS THE MOST APPROPRIATE EU WIDE MEASURE

Justification for the opinion of SEAC and RAC

Scope including derogations

Justification for the opinion of RAC

Summary of proposal:

The Dossier Submitter assessed two restriction options:

- **RO1: Implementation of a reference exposure value (REV).** Four values were assessed as restriction options (with their estimated cancer risk levels):

Option	Reference Exp. Value (µg Co / m³)	Excess Lifetime Risk
• RO1a:	10	$1*10^{-2}$,
• RO1b:	1	$1*10^{-3}$,
• RO1c:	0.1	$1*10^{-4}$ and
• RO1d:	0.01	$1*10^{-5}$.

  For RO1 the Dossier Submitter suggests a derogation for the use of the five cobalt salts as an additive in feeding stuff.

- **RO2: Minimum technical requirements for risk management measures (RMMs)** to be implemented for those uses of cobalt salts with the highest potential for worker exposure. Four sets are assessed as restriction options:
  - RO2a: mechanical ventilation,
  - RO2b: LEV,

[16] Directive 2004/37/EC – carcinogens or mutagens at work, https://osha.europa.eu/en/legislation/directives/directive-2004-37-ec-carcinogens-or-mutagens-at-work

- RO2c: closed systems or partially enclosed systems with LEV and
- RO2d: closed systems with integrated LEV.

A derogation for uses leading to exposure levels below 0.01 µg Co/m^3 (inhalable fraction) is included in all the options. Furthermore, a derogation is foreseen for the use as an additive in animal feed.

The following risk management options, other than restriction, were considered, but not assessed further by the Dossier Submitter:

1. Listing on **Annex XIV** of REACH

   The five cobalt salts were already recommended for inclusion in Annex XIV of REACH. However, it is noted that two of the sectors of highest concern (manufacture of cobalt salts, manufacture of other chemicals (intermediate uses of cobalt)) are not covered by authorisation.

2. A **binding occupational exposure limit value** (BOELV):

   A BOELV was in general considered as an applicable and effective risk management option for the five cobalt salts but, according to the Dossier Submitter, it was not suitable to address the identified risks due to the following reasons:

   - A BOELV does not consider the frequency and duration of the activities per year leading to exposure and consequently may require disproportionate risk management measures for activities that take place very rarely or would not be protective enough for activities taking place on a continuous basis.

   - The non-threshold nature of the hazard, where a BOELV may provide a false sense of safety as the basis of its derivation (and the remaining risk) is usually not communicated.

   - The length of time required for the development and implementation of a BOELV. The risk levels identified in the manufacture and use of the cobalt salts require that actions are taken to decrease workers exposure without undue delay.

3. **Voluntary industry action**:

   The Dossier Submitter does not consider any voluntary action to manage the risk being a practical and appropriate measure, given amongst others the number and variety of industrial sectors to be covered.

For all of the above-mentioned reasons, the Dossier Submitter considered the restriction with implementation of a REV of 0.01 µg Co/m^3 as the most appropriate regulatory risk management measure for the five cobalt salts within the scope.

RAC conclusions:

- The Dossier Submitter proposed a broad restriction covering almost all uses of the five cobalt salts. Instead of defining appropriate operational conditions and risk management measuress (which is not possible for so many sectors of use), the restriction proposal sets a reference exposure value (REV) of 0.01 µg Co/m^3 (RO1d) for the inhalable fraction, assuming 100% of the inhalable fraction is respirable. Besides the very conservative value actually proposed (see discussion in previous chapters), the REV is a new concept, e.g. it is meant to be adjusted for the duration and frequency of exposure, which has not been defined or used previously in REACH or any other European legislation applying to the workplace. If this concept is introduced, then it is likely to require practical guidance and clear differentiation from a DNEL or from a BOELV.
- As discussed above, RAC considers it more appropriate to implement limit values of 1 µg Co/m^3 (as 8 h TWA, for inhalable fraction) and 0.5 µg Co/m^3 (as 8 h TWA, for respirable fraction) rather than the proposed REV. Exposure levels below these limit values are considered protective from lung inflammation and secondary genotoxicity (which result in steeper increase in lung cancer risk above the limit values). They are also likely to protect from the other, non-cancer effects of cobalt.
- RAC notes that cobalt metal and other cobalt compounds can cause similar risks to the five cobalt salts covered by the restriction. RAC further notes that occupational exposure to cobalt is wider than just from the five cobalt salts within scope, and that not all the occupational cobalt exposures can be covered by a REACH restriction. These include for example exposures to cobalt fumes formed in hot processes, and cobalt exposures in waste management and the use of cobalt compounds as on-site intermediates.

Overall, RAC considers that a REACH restriction is at present the most appropriate regulatory measure to control the risks of the use of the five cobalt salts within scope in the EU. In addition, RAC recommends that work should be initiated to set a BOELV for cobalt and its compounds covering all occupational exposures.

The limit values proposed here by RAC can be considered applicable also for cobalt metal and other cobalt compounds releasing cobalt ions in contact with body fluids.

Regarding the proposed derogations that are included in RO1 and RO2 for the use as feed additives within the scope of Regulation (EC) no 1831/2003 on additives for use in animal nutrition, RAC concludes that within Regulation (EC) no 429/2008 on detailed rules for the implementation of Regulation (EC) No 1831/2003 a number of aspects are addressed concerning the “safety of use of the additive for users/workers” (especially annex II, subchapter 3.3), e.g.:

- Toxicological risk assessment for user/worker safety (effects on the respiratory system, effects on the eyes and skin, systemic toxicity)
- Measures to control exposure

However, the measures and assessments for safety for users/workers are neither specific for cancer risk nor for cobalt or cobalt salts. Additionally, the assessments foreseen by applicants are not likely to be quantitative and therefore the level of protection that will be achieved in the framework of Regulation (EC) No 1831/2003 is unknown**.** Therefore, from a risk assessment point of view, RAC does not consider this derogation justified.

Key elements underpinning the RAC conclusions:

The Dossier Submitter prepared this restriction proposal at the request of the Commission as risks were not adequately controlled from some uses (e.g. use of powder form in the surface plating) and as an alternative to authorisation of the five cobalt salts. For the five cobalt salts within the scope, restriction was considered more appropriate than authorisation, especially since with a restriction it is possible to cover also intermediate uses of cobalt salts in the manufacturing of other cobalt compounds, which are estimated to result in highest exposures. RAC agrees that in this sense restriction seems more appropriate than authorisation. As outlined in the conclusions above, for the five cobalt salts within the scope, RAC considers overall that a REACH restriction is at present the most appropriate regulatory measure to control the risks of their use in the EU.

However, as also outlined above, RAC additionally supports that a BOELV is derived for cobalt and its compounds. Based on the information received from consultation, approximately 50% of occupational exposures to carcinogenic cobalt compounds are not covered by the restriction. The majority of these exposures are caused by exposure to metallic cobalt or cobalt containing fumes formed in hard metal industry. Since metallic cobalt is also a lung carcinogen with a potency at least similar to cobalt salts, there is a need to regulate these exposures as well. RAC agrees that at present it might be faster to implement the limit value under REACH to control occupational exposure to the growing use of the five cobalt salts within scope. But in order to control other occupational cobalt exposures (including also exposures outside the scope of REACH like occupational exposure to process fumes, waste management and on-site intermediates), a BOELV is likely to be the more efficient and comprehensive regulatory measure in the long term, provided it gives the same level of protection as the limit value proposed by RAC.

The Dossier Submitter did not consider a BOELV a suitable option, amongst others because a BOELV would not consider the frequency and duration of exposure and could result in disproportionate risk management measures for activities which take place only rarely. RAC agrees that from a scientific perspective, frequency and duration of exposure is an important parameter when calculating the risk of cancer caused by cobalt salts. However, the practical implementation of a REV, which takes frequency and duration into account, would amount to a new practise in occupational hygiene and would need at a minimum practical guidance to monitor and implement this at workplaces by the employer and by the enforcement authorities.

It can be argued that it is undesirable to introduce further competing risk/exposure values into the workplace. In addition, as discussed under the hazard assessment, a frequency- and duration-adjusted reference value of 1 µg/m³ or higher may allow short term exposures (≥0.03-0.1 mg/m³), which have been associated with the occurrence of asthma. A frequency-

and duration-adjusted REV may also allow 8 h exposures above the breakpoint that may result in inflammation and secondary genotoxicity.

Another reason why the Dossier Submitter considered a restriction to be more appropriate than a BOELV was the non-threshold nature of the hazard, where a BOELV may provide a false sense of safety as the impact of socio-economic factors in the agreement process of a final limit value is not communicated. RAC agrees that the basis of individual BOELVs given under CMD is not always transparently communicated. However, RAC does not consider that this reasoning given by the Dossier Submitter applies specifically to the cobalt salts. It should be also noted that a REV proposed by the Dossier Submitter, is a new concept, and may have similar communication challenges. This was supported by the comments received from the consultation and Forum's advice. In several comments, REV was commonly mixed up with an 8 h TWA value.

Regarding the derogation proposed by the Dossiers Submitter for the use of cobalt salts as feed additives within the scope of Regulation (EC) no 1831/2003, RAC evaluated the risk assessment foreseen for users and workers in that regulation and in Regulation (EC) no 429/2008 on detailed rules for the implementation. In these two regulations no specifications for quantitative workplace risk assessment are considered, no specific risk management measures for occupational risks (including cancer risks) are implemented, and no specific requirements for cobalt compounds are available. RAC did not perform further evaluations and enquiries in this regard.

Justification for the opinion of SEAC

Summary of proposal:

See the opinion of SEAC.

SEAC conclusion(s):

See the opinion of SEAC.

Key elements underpinning the SEAC conclusion(s):

See the opinion of SEAC.

Effectiveness in reducing the identified risks

Justification for the opinion of RAC

Summary of proposal:

The Dossier Submitter only evaluated the impact of RO1 and RO2 in detail. Other regulatory options (see above) were not evaluated for their effectiveness in reducing the identified risks.

Improved control of exposure to the cobalt salts reduces the risk to individual workers and correspondingly the number of expected cancer cases. Independent of the restriction option and the exposure levels prevailing in each industrial sectors, the approach to estimate risk reductions and human health impacts is based on several assumptions about the effects of the regulatory action. The Dossier Submitter recognises that the assumptions made are uncertain. However, they provide an illustration of the potential risk reduction.

In the identification of the RMMs, the Dossier Submitter has considered the following aspects:

- Occupational hierarchy of controls.
- Effectiveness of individual RMMs.
- RMMs currently implemented in the different sectors of use to control exposure.

RO1

According to the Dossier Submitter assessment, the proposed REV should lead to a reduction of exposure and therefore a reduction in excess cancer risks in sectors where part of the industry is currently operating in risk levels higher than the REV. An indicative estimation of these benefits was done assuming that the:

- number of affected companies are the same as described for the economic impacts.
- average reduction in risk would be based on the effectiveness of the RMMs required to meet the REV.
- starting point for risk reduction is the RWC level for the first 10% of the companies (from the total number in that sector) and the typical exposure level to the rest of the affected companies.

According to the Dossier Submitter's analysis, the implementation of the restriction with a reference limit value of 0.01 µg/m³ (RO1d) would avoid 1.04 cancer cases/year whereas options RO1a-c would avoid 0.05-1.02 cancer cases per year.

RO2

The effectiveness of the RO2 was evaluated by the Dossier Submitter and is presented in the corresponding section of the Background Document.

RAC conclusions:

The effectiveness of the proposed restriction in reducing the identified risks is difficult to evaluate with certainty due to the identified uncertainties mainly in relation to exposure. The volumes of the cobalt salts used (see above) are expected to grow in the future. Therefore, it is possible that risk levels and/or exposed populations may increase. This has an impact on the effectiveness of the restriction. Two scenarios are considered possible by RAC:

- Greater turnover of cobalt salts per industrial site and worker would cause a potential for higher individual exposure and risk
- More sites with similar use of cobalt salts would cause a similar individual exposure and risk, given that RMMs and OCs are comparable, but a higher number of exposed workers

The limit values as proposed by RAC (1 µg Co/m³ (as 8 h TWA, for inhalable fraction) and 0.5 µg Co/m³ (as 8 h TWA, for respirable fraction)) can reduce the cancer risk below the level of 5.25×10^{-5} and are also effective in protecting from the other, non-cancer effects of cobalt. Because of the breakpoint in the dose response curve, higher exposure levels than the proposed REV are therefore as effective, as long as they do not exceed 1 µg Co/m³ (inhalable). **Exposure levels above 1 µg Co/m³ (inhalable), are not considered effective in reducing cancer risk or the risk of non-cancer pulmonary effects** (inflammation, decrease in lung function); for instance, an exposure level of 10 µg Co /m³ (as presented in RO1a) is associated with a cancer risk of 4.8×10^{-3}.

RAC notes that the restriction:

- Does not cover a number of relevant sources of occupational exposure to cobalt (e.g. exposures to cobalt fumes formed in hot processes, exposures in waste management and the use of cobalt compounds as on-site intermediates).
- Faces challenges related to the co-exposure to different cobalt compounds that are not covered by this restriction (e.g. Co metal, Co oxides).

On the other hand, the restriction could provide a limit exposure value for the protection for workers in a relative short period of time in the growing sectors using these five soluble cobalt salts.

Key elements underpinning the RAC conclusions:

RAC's bases the above conclusions on the following points:

- The Dossier Submitter stated in the impact assessment the uncertainty of many of the assumptions and the indicative nature of the impact assessment. RAC agrees with the Dossier Submitter's evaluation in this regard.
- During the consultation, most of the contributions doubted the effectiveness of RO1d (0.01 µg/m³) in reducing the identified risks. A number of contributions commented in favour of a BOELV. Other regulatory options were hardly commented. However, the contributions during consultation in this regard lack specific data to support the claims about the effectiveness of the proposed restriction. The most frequent claims were:
    - Technical impossibility to reduce the exposure below the proposed REV of 0.01 µg/m³.
    - Challenges in monitoring REV of 0.01 µg/m³ with the available monitoring methods not being sensitive enough.
    - Challenges in implementing an REV as a frequency- and duration-adjusted value.
- The RAC's proposal of 1.0 µg/m³ (inhalable fraction), 0.5 µg/m³ (respirable fraction) as an 8h TWA limit value was not discussed in the consultation.

Socio-economic impact

Justification for the opinion of SEAC

Costs

Summary of proposal:

See the opinion of SEAC.

SEAC conclusion(s):

See the opinion of SEAC.

Key elements underpinning the SEAC conclusion(s):

See the opinion of SEAC.

Benefits

Summary of proposal:

See the opinion of SEAC.

SEAC conclusion(s):

See the opinion of SEAC.

Key elements underpinning the SEAC conclusion(s):

See the opinion of SEAC.

Other impacts

Summary of proposal:

See the opinion of SEAC.

SEAC conclusion(s):

See the opinion of SEAC.

Key elements underpinning the SEAC conclusion(s):

See the opinion of SEAC.

Overall proportionality

Summary of proposal:

Proportionality:

The Dossier Submitter has assessed different REV and minimum technical requirements (four of each). The monetised results described under economic and human health impacts are depicted in Table 8 below. Furthermore, this table also summarises the qualitative information as regards practicality aspects, including technical and economic feasibility and availability of methods:

Table 8: Summary of restriction options

RO	Affected workers	Avoided cancer cases/year	Benefit/ year (€)	Cost/year (€)	Practicality
RO1					
RO1a	300	0.05	200 000	3 000	Demonstrated
RO1b	8 400	0.48	1 800 000	2 800 000	Demonstrated
RO1c	15 200	1.02	3 800 000	260 000 000	Possible
RO1d	18 900	1.04	3 800 000	370 000 000	Challenging
RO2					
RO2a	800	0.05	200 000	30 000	Demonstrated
RO2b	3 100	0.20	700 000	1 000 000	Demonstrated
RO2c	6 200	0.32	1 200 000	19 000 000	Possible (Uncertain for surface treatment)
RO2d	15 400	0.67	2 500 000	360 000 000	Uncertain
Derogations	**Affected workers**	**Cancer cases/year**	**Monetised HH impacts/ year (€)**	**Avoided Cost /year (€)**	**Practicality**
Derogation 1 (Animal feed)	0-990	0 - 0.0015	0 - 6 000	0 - 20 000 000	High
Derogation 2 (Exposure level <0.01)	5 -90	0.000001 - 0.00002	4 -80	400 - 6 000 000	High

As can be seen from Table 7 above, the applied methodology reveals net benefits. Only for RO1a and RO2a and for the derogations benefits are identified. However, in the Dossier Submitter's view, the methodology may not be sensitive enough to address a regulatory action that would only affect few companies with very limited requirements. Therefore, additional argumentation is needed to support the proposal.

In order to conclude on proportionality, the Dossier Submitter concludes for RO1 and RO2 the following:

RO1: The **advantages** of implementing a reference exposure value in the CSA and SDS together with the suggested derogation on animal feed is that these values will be communicated down the supply chain through the SDS, ensuring that the risks are known across all sectors of use. Furthermore, this is understood being the minimum regulatory intervention as registrants and downstream users may decide individually upon the most adequate RMMs to be implemented at their worksite to reduce exposure to the required level. According to the Dossier Submitter, this is in line with the underlying principles of REACH. The main **drawback** of RO1 is that the reduction in risk may be theoretically achieved with the use of personal protective equipment (PPE), even when appropriate technical measures are available and feasible to be implemented.

RO2: The **advantages** of implementing minimum technical requirements with the suggested derogations for animal feed additives and for activities with very low exposure is that an adequate set of technical measures is to be implemented throughout the industry following the hierarchy of controls. The drawbacks are, that this option will not address the problem of

communicating the risks of the non-threshold carcinogenicity of the substances. Furthermore, the actual effectiveness of RMMs will differ. Also, targeting of more specific RMMs for each sector of use is not possible, due to the number of sectors and the lack of specific information for each of them [to be adapted if more specific information is provided in the PC]. Lastly, the risk reduction effectiveness is limited since it addresses exclusively the risks resulting from exposure to the cobalt salts in certain activities (those with highest potential of exposure).

Due to the above considerations, the Dossier Submitter concludes that RO1 is preferable to RO2 as regards the question whether or not a restriction is the most appropriate EU-wide measure. Within the four different RO1, the Dossier Submitter regards RO1d being the most appropriate RMM. The other restriction options assessed would not ensure achieving this high level of protection. RAC challenged this assessment of the Dossiers Submitter during the opinion making process.

RAC and SEAC conclusions:

RAC's view:

Based on the evaluation of the available data, RAC concludes as follows:

- The superiority of the proposed regulatory option RO1d (over the other regulatory options) in reducing the risks is not demonstrated.
  - ➔ The proposed REV of 0.01 µg/m³ (as inhalable dust, weighted over frequency and duration) does not provide a higher level of protection. Other regulatory options (0.1 or 1 µg Co/m³ as 8h TWA limit values, or a BOELV) can also provide a high level of protection, but not 10 µg Co/m³. This latter level is likely to result also in non-cancer health hazards (decrease in lung function, inflammation and respiratory sensitization), and a significantly higher cancer risk.
  - ➔ Practicality aspects make RO1d extremely challenging.
- The proposed derogations will not provide a comparable level of worker protection within the framework of Regulation (EC) no 1831/2003.
  - ➔ The risk management for workers/users within the framework of Regulation (EC) no 1831/2003 lacks concrete RMMs and level of protection.

Key elements underpinning the RAC and SEAC conclusions:

Uncertainties in the proportionality section

The uncertainties in the proportionality section are highlighted above and are summarised in the section on uncertainties and in the chapter "Uncertainties in the risk characterisation" of this opinion.

Practicality, incl. enforceability

Justification for the opinion of RAC and SEAC

Summary of proposal:

The Dossier Submitter considers practicality and enforceability of the restriction proposal on several levels (Manufacturers and importers, suppliers, downstream users) – mostly by

checking safety data sheets and visual control of workplaces – as possible and practical. This assessment is believed to be valid for RO1 and RO2. A difference is mainly seen for the REV to be chosen. Obviously, practicality (and also enforceability) is more complex when the REV is decreasing.

The Forum's advice is clear about the practicability and enforceability of RO1d (0.01 µg Co/ m^3) and addresses mainly three points being considered as major problems for enforceability of this Dossier Submitter's proposal for restriction:

- Quantitative analysis of cobalt in the workplace air is restrained by possible interference with other cobalt compounds, the fact that the practicability of the available methods for airborne cobalt compounds is not proven yet, and that only a limited number of methods show a Level of Quantification that is sufficiently low.
- This restriction is not practicable and enforceable due to a conflict resulting from the REV and its unclear relation to limit values according to OSH requirements (and national implementation in the Member States). At the moment, the OELs (as shown in the dossier) are higher than the REV. According to the Forum advice, it is not possible to enforce two different (limit) values. RAC notes that this is not specific for the cobalt salts, but concerns all those substances for which the OEL and $DNEL_{worker}$ are not similar.
- For RO1d it will not be really practicable for REACH inspectors to check this. It will be possible to check the presence of a monitoring system but for a more deep inspection on workplaces and occupational exposure specific knowledge is needed.

Other aspects of the restriction proposal (e.g. conditions 1a – 1c, derogation for feeding stuff) are considered as practicable and enforceable by the Forum.

RAC and SEAC conclusions:

RAC's view:

RAC is of the opinion (in line with the Forum's advice and a relevant number of contributions in the consultation) that implementation, enforcement and especially monitoring of the restriction as proposed by the Dossier Submitter will be extremely challenging. Especially contributions of industry in the consultation point in the direction that:

- the REV of 0.01µg/m^3 is not achievable by many of the affected industry sectors
- neither in-house monitoring as performed by industry nor monitoring by enforcement authorities will be able to show compliance (or non-compliance) with the REV.

On request of RAC the Forum provided additional advice on RAC's proposal of a limit value as an 8h TWA instead of the original reference exposure value proposed by the Dossier Submitter. For this approach, Forum gave a favourable advice. The limit values as proposed by RAC seem enforceable and overall practical. RAC considers the proposal of 1 µg Co/m^3 (as 8 h TWA, for inhalable fraction) and 0.5 µg Co/m^3 (as 8 h TWA, for respirable fraction) as limit values for the five cobalt salts as practical and enforceable.

Additionally, it should be noted that for compliance of the 0.5 µg/m^3 (respirable fraction) as an 8h TWA limit value it is not in every case necessary to monitor the respirable fraction. For reasons of practicability, RAC considers it sufficient to demonstrate:

- compliance with the 1.0 µg/m³ (inhalable fraction) as an 8h TWA limit value by workplace air monitoring and

- that the respirable fraction is less than 50% of the inhalable fraction for that particular use.

Key elements underpinning the RAC and SEAC conclusions:

RAC's view:

RAC's conclusion is based on

- some assessments of the Dossier Submitter,
- the advice of Forum regarding the Dossier Submitter's proposal and RAC's proposal, as summarised above, and
- a relevant number of critical contributions to the consultation by affected industry (associations, individual companies)

All these contributions (even the assessment of the Dossier Submitter) refer to the original proposal of the Dossier Submitter and show clearly that the Dossier Submitter proposal for a REV of 0.01 µg/m³ is at least challenging regarding practicality and enforceability.

The Forum working group Enforceability of Restrictions considers that there are available methods to check limit values of 10 and 1 µg/m³ (inhalable fraction) as presented in RO1a and RO1b, respectively. ISO 15202 seems to deliver for 10 µg Co /m³ and the ISO 30011 seems to deliver for a limit value of 1 µg Co /m³. The Forum WG does not see major technical obstacles for the implementation of both values and to set a protective environment for workers. Industry has available methodology to demonstrate that the air quality of the workplace is at the required level. Enforcement authorities could check this information from industry or set contracts with laboratories to undertake these studies. From this it is clear that RAC's proposal for 1 µg Co/m³ (inhalable fraction) as an 8h TWA limit value is practical and enforceable.

Only a very limited number of contributions in consultation addressed the practicality of the REVs presented in RO1a and RO1b:

- 10 µg/m³ (inhalable fraction) is regarded as technically and economically feasible
- 1 µg/m³ (inhalable fraction) might be technically feasible, however, economically challenging

Monitorability

Justification for the opinion of RAC and SEAC

Summary of proposal:

The proposed restriction applies to the marketing and use of the five cobalt salts as substances on their own or in mixtures in a concentration equal or above 0.01% by weight. Monitorability in this regard seems possible as confirmed also in the Forum's advice.

Regarding the monitoring at workplaces the Dossier Submitter concludes that both assessed restriction options, RO1 and RO2, can be monitored by enforcement authorities. Any

monitoring activities need to take into account the use of adequate analytical methods, depending on the REV.

RAC and SEAC conclusions:

RAC's view:

Taking into account the information provided in the Restriction dossier, information gathered during the consultation and the advice given by the Forum, RAC concludes that the monitorability of the proposed REV of 0.01 µg/m³ is at least challenging, considering the currently available analytical methodologies and the lack of sufficient expertise in Member States.

A level of 1.0 µg/m³ (inhalable fraction) and 0.5 µg/m³ (respirable fraction) as an 8h TWA limit (RAC's proposal) value is less challenging to monitor as confirmed by the additional Forum advice (see above). Forum confirms the availability of monitoring methods for workplace air for the proposed values for industry and authorities. The co-exposure of the cobalt salts with other cobalt species may still present a challenge, though.

RAC's and SEAC's reasoning is given below.

Key elements underpinning the RAC and SEAC conclusions:

RAC's and SEAC's view:

- According to information provided in the Restriction dossier, provided by Forum and monitoring experts, RAC and SEAC note that the proposed REV (RO1d, 0.01 µg Co/m³ weighted over frequency and duration) value can be monitored in theory, but this is regarded as very challenging in practice. With the available methods, monitoring is most probably possible only at very few workplaces at present; however, RAC and SEAC note that adequate analytical methods might be developed in future.
- Forum states that the equipment needed to perform the workplace air monitoring for RO1d is expensive and it is expected that there are currently only few laboratories in the EU that can do the respective testing. This statement was confirmed by comments received during the consultation.
- Forum considers that there are available methods to check values according to RO1a and RO1b. ISO 15202 seems to be sufficiently sensitive for 10 µg Co /m³ (RO1a) and the ISO 30011 for 1 µg Co /m³ (RO1b). Forum does not see major technical obstacles for the implementation of both values. Industry has available methodology to demonstrate that the air quality of the workplace is at the required level. Enforcement authorities could check this information from industry or set contracts with laboratories to undertake these studies.
- From the previous bullet point it follows that the limit value proposed by RAC (1.0 µg/m³ (inhalable fraction), 0.5 µg/m³ (respirable fraction) as an 8h TWA limit value) is monitorable.
- Here it should be noted again, that for compliance with the proposed limit values monitoring of the respirable fraction is not always necessary.

UNCERTAINTIES IN THE EVALUATION OF RAC AND SEAC

RAC

Summary of proposal:

Uncertainties and their influence on the risk characterisation are described in detail in the chapter "Uncertainties in the risk characterisation" above. RAC identified additional uncertainties in the chapters on:

- Justifications whether the suggested restriction is the most appropriate EU wide measure.
- Effectiveness in reducing the identified risks.
- Practicality, incl. enforceability.
- Monitorability.

The uncertainties in the above chapters are less quantifiable than those evaluated in the chapter on risk characterisation. Also the influence (over or underestimation of the impact) of these uncertainties is less clear.

RAC conclusions:

RAC concludes that the uncertainties of the proposed restriction by the Dossier Submitter are significant. These uncertainties are not limited to single aspects of the proposal but affect a relevant number of different aspects of this dossier.

The main uncertainties of the Dossier Submitter's proposal (RO1d) are related to:

- Appropriateness of the best EU wide measure: setting of a BOELV for cobalt and cobalt compounds is also considered as a possible regulatory option.
- Effectiveness in reducing the identified risks:
    - the impact and effectiveness of RMMs is uncertain as only limited information is available on this.
    - the experience on similar restrictions focusing on occupational exposures is very limited.
- Enforceability: the Forum's advice challenges the practicality of the proposed REV of 0.01 µg/m³.
- Monitorability: the available methods for workplace air monitoring can hardly achieve the necessary limit of quantification for monitoring compliance to the REV of 0.01 µg/m³.

RAC concludes also, that the restriction as proposed by the Dossier Submitter:

- does not cover a number of relevant sources of occupational exposure to cobalt (e.g. exposures to cobalt fumes formed in hot processes, exposures in waste management and the use of cobalt compounds as on-site intermediates);
- faces challenges related to the co-exposure to different cobalt compounds that are not covered by this restriction (e.g. cobalt metal, cobalt oxides).

Some of these uncertainties are addressed by RAC's proposal for a breakpoint approach and an 8h TWA limit value (1.0 µg/m³ (inhalable fraction) / 0.5 µg/m³ (respirable fraction)) for the restriction (rather than a linear approach and a REV that is to be weighted over frequency

and duration). Other issues/uncertainties can be addressed by RAC's additional proposal to the European Commission to derive a binding occupational exposure limit value (BOELV) for cobalt and its compounds according to Directive 2004/37/EC on the protection of workers from the risks related to exposure to carcinogens or mutagens at work (CMD). This value should be identical to RAC's proposed limit value of 1.0 µg/m³ (inhalable fraction) and 0.5 µg/m³ (respirable fraction) as an 8h TWA limit value to ensure a similar level of protection to workers from exposure to the cobalt salts.

However, some uncertainties remain with regard to the effectiveness in reducing the identified risks, related to the limited experience on similar restrictions focusing on occupational exposures and to the impact and effectiveness of RMMs to be implemented by industry.

Key elements underpinning the RAC conclusions:

RAC's conclusions on uncertainties are presented in the most affected chapters of this opinion:

- Uncertainties in the risk characterisation (especially in exposure assessment)
- Justifications whether the suggested restriction is the most appropriate EU wide measure
- Effectiveness in reducing the identified risks
- Practicality, incl. enforceability
- Monitorability

SEAC

Summary of proposal:

See the opinion of SEAC.

SEAC conclusion(s):

See the opinion of SEAC.

Key elements underpinning the SEAC conclusion(s):

See the opinion of SEAC.