**Committee for Risk Assessment (RAC)**

ANNEX 2

**Response to comments document (RCOM)**

on the Proposal by the European Chemical Agency (ECHA)

in support of occupational exposure limit values for nickel and its compounds in the workplace

**Nickel and its compounds**

**EC number: -**

**CAS number: -**

ECHA/RAC/A77-0-0000001412-86-189/F

**9 March 2018**

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| **Ref.** | **Date/Name/Org.** | **Type of comment** |
| 5 | **Date/Time:**  2017/10/31 19:45  **Type:**  BehalfOfAnOrganisation  **Organization name:**  BDI e.V.  **Country:** Germany  **Non-confidential attachment:**  Comment on Ni OEL proposal.pdf | **Comment**  *(See attachment)* |
| **Dossier Submitter response**  Thank for your comment.  ECHA would like to explain the details of the assessment factors used for the respirable OEL:  The human equivalence concentration (HEC) represents the exposure concentration for humans adjusted for dosimetric differences between experimental animal species (in this case the rat) and humans. Since the HEC calculation reflects the toxicokinetic interspecies differences, an additional assessment factor (AF) is not required. Toxicodynamic interspecies differences are not considered in HEC. However, it is assumed that the rat is not less sensitive to different nickel compounds than humans, as supported by epidemiological data and therefore an additional assessment factor for toxicodynamic differences was not applied. The additional assessment factor of 5 is applied to overcome uncertainties related to intraworker difference (toxicokinetic and toxicodynamic), which are not addressed in the HEC calculation. Therefore, this AF does not represent a duplication of AFs for the OEL derived for the respirable fraction of nickel and compounds.  ECHA is aware of the ongoing discussion of the German AGS related to the inhalable OEL for nickel compounds at the time the ECHA documents was drafted. Unfortunately, the proposal was not published and is therefore not reflected in the ECHA document. However, ECHA reconsidered the rounding for the inhalable fraction of 0.027 mg Ni/m³ to propose now 0.03 mg Ni/m³ for the inhalable OEL. |
| **RAC Rapporteurs comments**  Thank you for your comment. |
| **Ref.** | **Date/Name/Org.** | **Type of comment** |
| 8 | **Date/Time:**  2017/11/06 13:12  **Type:**  BehalfOfAnOrganisation  **Organization name:**  [Confidential]  **Country:** Italy | **Comment**  Some different nickel salts are used in Europe by the semiconductor industry in a process of metallizing silicon wafers (for both the whole wafer surface and the bonding pad areas only) leading to the development of semiconductor components, with major advantages in performance, process stability, application diversification, costs and competitive advantages.  The semiconductor products obtained are marketed globally in high-volume markets, characterized by higher competition. They have a leading position in the world and they ensure European leadership in the sector.  Nickel salts are typically used in electro less plating processes taking place in closed equipment. There is no potential exposure to the worker during normal and routine semiconductor manufacturing as the nickel compounds are within a closed system manufacturing equipment tool, within itself a clean room environment. Local exhaust ventilation, safe locking and unlocking chemicals containers and double piping automatic delivering systems, automatic wafer loading and unloading, controlled spent solution waste management and equipment flushing before opening for maintenance are ensured. Moreover operations take place in restricted access area only and PPE are worn, as a further precautionary practice.  Within the various European sites located in Italy and France regular industrial hygiene monitoring are conducted (usually twice/year per site and per manufacturing area where the Nickel salts area used).  While most of the values are found below detection limits, ECHA can conclude that all measured values were below local applicable TLV and definitely all values were < 0.0043 mg/m3  In 2016 a total of 8 air sampling campaigns (in 3 sites located in Italy and France) were conducted covering all the interested working areas and maintenance operations. |
| **Dossier Submitter response**  Thank you for your information and your interest in this process.  Section 5.2 of the ECHA proposal describing uses is in line with this comment. The plating takes place in closed systems, but during charging and maintenance there is potential for exposure. The exposure values are taken from registration information provided by industry. |
| **RAC Rapporteurs comments**  Thank you for your comment. |
| **Ref.** | **Date/Name/Org.** | **Type of comment** |
| 10 | **Date/Time:**  2017/11/06 20:27  **Type:**  BehalfOfAnOrganisation  **Organization name:**  European Committee for Surface Treatment  **Country:** Germany  **Non-confidential attachment:**  2017-11-06 Comment on the Proposal by the European Chemical Agency\_final\_Version.docx | **Comment**  The following comments are conclusions from more detailed discussions shown in the attached document  p. 15 - 19:  Comment on existing exposure limits:  Report of current exposure limits in European countries is without substantial information due to missing details about the specific measurement requirements in each country.  p. 42 - 43:  Comment on monitoring of external exposure:  The applicability of analytical methods reported is questionable. There is no statistical approach to reproducibility and comparability. Furthermore, the proposal lacks a discussion of matrix effects or possible sampling deviation. The proposal should thoroughly discuss the informational value of real analysis at workplaces.  p. 43 - 49:  Comment on monitoring of internal exposure (biomonitoring):  The data of external exposure reported in the proposal are not valid. The reported studies differ a lot and show significant lack of data needed for conclusions. With that the proposal misses its own requirement, the “evaluation of the scientific relevance” by neglecting sound science approaches in evaluating the applicability of the data reported.  The data evaluation shows clearly that the conclusions (relations) will not be valid in the ordinary range of exposure level of modern workplaces.  p. 19 - 34:  Comment on production and use information:  The proposal fails to describe in detail the uses, resulting in overestimation of potential exposure routes. At least as regards the electroplating sector, the proposal needs to be revised intensively.  Given that the proposal does not take into account the interactions with other regulation, it does not provide sufficient information to establish a well-founded opinion or to base new measures on.  General comment:  The proposal intends to provide a base for assessing occupational exposure limits for Nickel and its compounds. Based on the above, CETS is of the opinion that more scientifically sound work is needed to achieve reliable conclusions. The data concerning exposure, analytical methods and common uses presented in the proposal do not fulfil the requirements for a reliable decision on valid occupational exposure limits.  CETS hereby offers its cooperation in investigating proper data and information to help find meaningful and appropriate exposure limits.  Given the limited timeframe of the consultation, not all toxicological presentations could be assessed. This would have required consultations of experts that take more time than that available.  CETS regrets that smaller associations are not given enough time to verify the entire consultation content, including those parts that are out of the association’s general scope. |
| **Dossier Submitter response**  Thank you for your comments. ECHA appreciates your concern about the length of the public consultation, however, the deadline to deliver the opinion of RAC to the European Commission (26 March 2018) unfortunately did not allow for a longer public consultation.  Please find here explanations related to your more detailed comments on:  *Existing exposure limits.*  The report on existing OELs in the different European countries only provides contextual information to the proposed change on the limit value, making clear the current requirements in each country. They do not show any actual exposure levels in different European countries but the “maximum level” allowed for a shift. The reports on actual levels of exposure in different activities appear in Section 5 of the document and they explain or make reference to type of sampling, method used etc.  *Monitoring of external exposure*  The analytical methods reported in the document are validated against the European Standard 482: Workplace exposure. General requirements for the performance of procedures for the measurement of chemical agents or have the potential to meet the requirements of it (as they were validated for a higher limit value)  The standard gives the requirements that the analytical method need to fulfil, when the measured data is to be compared with an occupational limit value. To make this clear one sentence stating that the methods are validated and that the validation data can be consulted either in the actual published analytical methods and /or in the “methods sheets” published at the Gestis database of analytical methods has been included in the opinion.  *Biomonitoring*  The data on internal exposure provided in the ECHA proposal consist of published information and have been included in order to give a comprehensive overview of the exposure of workers to nickel and compounds. However, the final RAC opinion and (the background document) do not recommend the establishment of a biological limit value. The reason for not maintaining the BGV is the high variability of background levels of nickel in urine between the different populations in Europe.  *Production and use information*  The information on uses given in the document is based on information provided by industry (through the lead REACH registrants for nickel and inorganic compounds), and through the Nickel Institute. The exposure data associated with the uses is taken from registration information. However, this information is not crucial for the science-based setting of occupational exposure levels. |
| **RAC Rapporteurs comments**  Thank you for your comment. |
| **Ref.** | **Date/Name/Org.** | **Type of comment** |
| 11 | **Date/Time:**  2017/11/06 22:39  **Type:**  BehalfOfAnOrganisation  **Organization name:**  NiPERA  **Country:** United States  **Non-confidential attachment:**  171106-NiPERA comments on the ECHA Proposal for Ni OELs-.pdf | **Comment**  *(See attachment)* |
| **Dossier Submitter response**  Thank you for your comments.  *Main comments*  *As regards the main comments on section 7.9 Mode of Action*   * The comments on a proposed MoA supporting an indirect genotoxicity MoA are noted as are those on the combined MoA and dose response functions to further support the OEL, based on a MoA threshold. The ECHA proposal addresses both of these points although it does not include the specific proposal from NiPERA. The section on MoA has been elaborated to address the MoA in more detail.   *As regards the main comments on human cancer section 7.7.1:*   * Text added acknowledging that the largest cohorts were able to detect small lung cancer increases with narrow confidence intervals. * As regards the detailed comments related on temporal trends in Ni exposure over decades in the industry as general and comparison of those to the multiplication factors used in the Kristiansand cohort a more detailed description was added for the Kristiansand methodology and a separate description of the industrial trend was included. However, it was not possible to perform a direct comparison to verify the appropriateness of the multiplication factors used. * As regards the comment regarding total Ni exposure and the water soluble Ni exposure in the cumulative exposure category from the Kristiansand cohort used in deriving the OEL for inhalable factor, ECHA acknowledges that exposure to total Ni was indeed higher that exposure to water soluble Ni. This is clarified in chapter 8.2.1 [and the rounding is consequently done upwards].   *As regards the main comments on section 7.7.1 Carcinogenicity*   * Thank you for your extensive analysis of the data. ECHA reconsidered the rounding for the inhalable fraction of 0.027 mg Ni/m³ and propose now 0.03 mg Ni/m³ for the inhalable OEL**.**   *As regards the main comments on section 8.1.4*   * More details added on chest radiographic findings in Kristiansand workers (chapter 7.3.1)   *As regards the main comments on sections 8.3 Notations*   * The notation is for sensitisation (SEN) because nickel and all its compounds are skin sensitisers, and some are also respiratory sensitisers. The notation is simply for “sensitisation” and does not differentiate between skin or respiratory. Thus the notation is correct. The ECHA proposal has been revised for clarification and the notation remains as SEN.   *Detailed comments*  *As regards the detailed comments on sections 7.1 – 7.6 (14 comments)*   * All of the comments have been reviewed and in most cases implemented by elaborating the text or revising for clarification.   *As regards the detailed comments on human cancer section 7.7.1:*   * Adding the information on which sampler and/or aerosol fraction was used in assessing exposure in each cohort was not possible. However, a clarification was added that all data in Oller et al 2014 referred to inhalable fraction. * Clarification added on the nasal cancer cases of Pavela et al 2017. * Mining and non-sinter smelter sub-cohorts of Ontario added to text and tables 44-46.   *Detailed comments on exposure monitoring section 6*  Regarding the inclusion of recommendations on sampling strategy in the Annex I, this is considered out of the scope of the Annex. The Annex intends to provide enough data to support the proposed revised limit values, for that it is important to understand whether there are analytical methods that could demonstrate that the exposure is below the limit value.  However, including recommendations on sampling strategy do not add any value in terms of deciding whether the proposed OEL is feasible in terms of measurement. It is acknowledged that further harmonisation at EU level regarding exposure sampling would be desirable but this is considered a broad issue to be tackled in general (and maybe in a different forum).  Regarding the analytical methods the list intends to show methods that can potentially reach the proposed limit values (ideally able to determine 0,1 of the OEL after a reasonable sampling time). As acknowledged in the introductory text to the table, the data for the current scope of the analytical methods are included (e.g. soluble/ inorganic compounds etc) and the LOQ calculated use the flow rate of the sampler recommended in the method. The methods could be modified but ECHA included the ones available at the moment so it is clear that the validation data.  Already two of the methods included in the table (MDHS 42/2 and BGI 505-10-3) allow to measure concentrations of 0.1 of the OEL in (2 to 4 hours sampling time) and are validated following sampling standards. Thus it is considered it is feasible to perform measurements to show compliance with the proposed OEL (including the one for respirable fraction). Naturally, some of currently available methods would need to be discarded (or updated and modified) to be used for this revised values, as they were optimised and validated for different concentration ranges.  *Editorial and clarification comments*  Section 5.3.1 Table 11 (and other sections mentioned in the comment): additional information (aerosol fractions) has been provided as much as possible.  For the comment on welding generating complex nickel oxides, this is already mentioned in the opening paragraph describing welding. |
| **RAC Rapporteurs comments**  Thank you for your comment. |
| **Ref.** | **Date/Name/Org.** | **Type of comment** |
| 15 | **Date/Time:**  2017/11/07 11:59  **Type:**  BehalfOfAnOrganisation  **Organization name:**  Austrian Workers' Compensation Board (AUVA)  **Country:** Austria | **Comment**  The proposal for occupational exposure limit values for nickel compounds is refused with regard to poorly soluble nickel compounds. (Not refused is the OEL for nickel metal and soluble nickel compounds.)  The aim of the proposal is to support the derivation of an OEL in accordance with Directive 2004/37/EC (CMD).  *GENERAL AND SPECIFIC COMMENTS:*  The current scientific knowledge is not such that a level can be established below which risks to health cease to exist (recital 11 of CMD); this is the case for less-soluble nickel compounds to a quite relevant extent. To date, there is no clear answer to the question if cancer is induced by these compounds via a threshold or non-threshold MoA. As a conservative approach a non-threshold MoA has to be presumed.  In particular, regarding exposure to carcinogens, the precautionary principle should be applied in the protection of workers’ health (recital 14 of CMD). The employer has to ensure that the level of exposure of workers is reduced to a low level as is technically possible (CMD, Article 5(3)). [In respect to technical possibility, the framework directive 89/391/EEC explicitly emphasizes that the improvement of workers’ safety and health at work is NOT to be subordinated to purely economic considerations (13th recital of that Directive)].  To support and to guide this minimization obligation, an OEL representing a VERY low cancer risk has to be established.  In the related field of potentially dangerous products and consumer-use chemicals the European Commission already has established a benchmark for assigning the terms “serious risk”, “high risk”, “medium risk” and finally “low risk” (Commission Decision 2010/15/EU of 16.12.2009, OJ No L 22, 26.1.2010). Cancer from contact with substances is classified as a hazard of the (highest) Severity Group 4. This Commission Decision provides (in its table 4) the combination of the severity of harm and its probability: Only if the probability of cancer causation is LESS THAN 1:1,000,000 (related to the exposure duration) the risk is judged to be “low risk”!  This clearly shows that strict criteria have to be met, and cancer risks have to be in the order of 1:1,000,000 and preferable lower to be acceptable.  In significant European member states a risk based approach is implemented (DE, NL) for controlling the exposure to carcinogens at the workplace. The acceptable cancer risk in these concepts is 1:1,000,000 per work year, resulting in an “acceptable” cancer risk of 4:100,000 per work lifetime.  A work lifetime cancer risk of 4:100,000 is a reasonable and necessary concretion of the minimization principle (and of recital 4 of CMD), being the main objective of the CMD.  Besides that, also REACH demands that a low risk must be ensured when using a carcinogenic substance. Guidance documents published by ECHA (e.g. Chapter R.8) suggest an excess lifetime cancer risk of the same order of magnitude as outlined above.  Therefore, an OEL associated with a work lifetime cancer risk NOT HIGHER THAN 4:100,000 has to be required.  In the case of less-soluble nickel compounds (e.g. nickel subsulphide, nickel oxide, nickel sulphide) the exposure-risk relationship derived in the AGS approach (2017) shows a work lifetime cancer risk of 4:100,000 associated with a respirable Ni-concentration of 1 µg Ni/m³ (rounded from 0.8 µg Ni/m³). This takes into account the indirect genotoxicity.  In contrast, an OEL of 5 µg Ni/m³, as proposed by ECHA, would result in a work lifetime cancer risk of approximately 3:10,000 (instead of 4:100,000) for less-soluble nickel compounds.  Therefore, an OEL of 1 µg Ni/m³ should be established for less-soluble nickel compounds.  In every case, it has to be stated explicitly that the respirable fraction does not include nanoparticles, and the OEL for the respirable fraction does not apply to nanoparticles.  *REMARKS:*  A consistent level of protection from the risks related to carcinogens or mutagens has to be established for the EU as a whole (recital 4 of CMD). In should be noted that “risk” means the likelihood (probability) that the potential for harm will be attained under the conditions of use and/or exposure (Directive 98/24/EC, Article 2; to be applied according to Article 1(3) of that Directive).  Adopting an opinion on an OEL for nickel compounds in accordance with the CMD (as declared in the mandate) necessarily has to take into account political and socioeconomic issues. Neither the ECHA nor the RAC is competent to argue on the time scale of implementation, on transitional measures (if necessary) or on other matters referring the regulatory enforcement of OELs. The partial questionable handling of scientific findings and omitting the risk-based approach creates the impression that also (undeclared) non-scientific elements are incorporated into the proposal. |
| **Dossier Submitter response**  Thank you for your comment.  It is outside the remit of ECHA or RAC to comment on, or to determine, the acceptability of cancer risks. ECHA considers a mode of action-based threshold[[1]](#footnote-1) for nickel and compounds in respect to lung tumour formation in rats and humans in its derivation of OELs. At nickel and its compounds exposures below the resulting proposal for a limit value, no significant residual cancer risk is expected for workers. The justification is presented in the Background Document.  It should be noted that the mandate of RAC is to evaluate the scientific relevance of occupational limit values for nickel and its compounds, and to assess the most recent and relevant scientific information. The RAC-opinion on nickel and its compounds is used by the Commission to set limit values for the protection of workers from exposure to chemical risks, as per Directive 2004/37/EC. The Commission takes socio-economic and technical feasibility factors into account in their legislative procedure for developing EU OELs.  REMARKS: Independence is extremely important to ECHA. ECHA’s work is based on science and it is of the utmost importance to guarantee the independence of the ECHA’s staff and Committee members nominated by the Members States. All ECHA staff have completed a detailed declaration of interest before starting to work, these declarations are updated and examined at least annually. Similarly the experts in the scientific Committees are screened against targeted eligibility criteria. Their published Declarations of Absence of Conflict of interest are examined and updated annually. In addition to these regular Declarations of Interest, every Committee meeting starts with an oral declaration on any specific interests related to the agenda items to be discussed. |
| **RAC Rapporteurs comments**  Thank you for your comment. |
| **Ref.** | **Date/Name/Org.** | **Type of comment** |
| 16 | **Date/Time:**  2017/11/07 12:08  **Type:**  BehalfOfAnOrganisation  **Organization name:**  Nickel Institute  **Country:** Belgium  **Non-confidential attachment:**  2017-11-07 NI comments.zip | **Comment**  We herewith provide our comments attached in a formatted version. As our comments includes tables and formulas we were not able to insert it into the text box. For your convenience, we include the word version as well. |
| **Dossier Submitter response**  Thank you for your comments and your interest in the process.  ECHA considers a threshold based mode of action for nickel and compounds in respect to lung tumour formation in rats and humans. This assumption is based on detailed scientific analysis of the available *in vitro* and *in vivo* data. The proposed OELs are based on conservative health-based assumptions taking all available data into account.  *Comments on compliance approaches.*  Please see reply to comment number 11 *(Detailed comments on exposure monitoring section 6)*  *Comments on analytical methods for nickel in air*  Please see reply to comment number 11 *(Detailed comments on exposure monitoring section 6)*  Also, please note that the table included in the background document already contains several methods that can achieve 10% of the OEL and therefore allow to measure concentrations of 0.1 of the OEL for respirable fraction in (2 to 4 hours sampling time) and which are validated following sampling standards.  The intention of the table is to show that these concentrations can be measured. The fact that some of the current methods would need modification to fulfil the EN 482 is expected as these had been validated and optimised for the current OELs. Several of the methods fulfil already the requirements of the EN 482 by using a sampler working at a higher flow rate.  All the analytical methods proposed comply with analytical techniques routinely used for workplace assessments and among the methods that already fulfil the EN 482 requirements different analytical techniques are covered (including for instance GFAAS).  Regarding the speciation issues the OEL is proposed for Ni and its compounds (incl. metallic nickel), so only one extraction step is foreseen. |
| **RAC Rapporteurs comments**  Thank you for your comment. |
| **Ref.** | **Date/Name/Org.** | **Type of comment** |
| 20 | **Date/Time:**  2017/11/07 18:19  **Type:**  BehalfOfAnOrganisation  **Organization name:**  B.Mason & Sons Ltd  **Country:** United Kingdom  **Non-confidential attachment:**  Nickel comments .docx | **Comment**  *(See attachment)* |
| **Dossier Submitter response**  Thank you for your comment.  ECHA would like to clarify that in the example referring to a safety data sheet, an alloy is a special mixture and whether or not nickel (and in what concentration) has to be indicated in the SDS is defined in the REACH Regulation Annex II Section 3.2. Raising or lowering the OEL has no impact on this. If the substance has to be included then its OEL is indicated in Section 8, so changing the OEL means indicating a different value here, but has no impact on whether it has to be included in Section 3.2.  An occupational exposure limit refers to an upper limit on the acceptable concentration of a hazardous substance in workplace air. It is not a clear question to ask what impact lowering an OEL has on products with low levels of impurities of the substance subject to the OEL, as it depends on how that product is used in the workplace, how much of the relevant substance might be released during the use, and what the resulting exposure to workers might be. Essentially the content (whether high or low levels of nickel) is not as important as how the product is used, the workplace exposure has to be below the OEL. |
| **RAC Rapporteurs comments**  Thank you for your comment. |
| **Ref.** | **Date/Name/Org.** | **Type of comment** |
| M1 | **Date/Time:**  Monday, November 06, 2017 4:07 PM  **Type:**  Member State  **Organization name:**  Ministero del Lavoro e delle Politiche sociali  **Country:**  Italy | **Comment** |
| **Dossier Submitter response**  Thank you for your support.  Please note that the CAS and EC numbers of different nickel compounds can be found in the Appendix 2 of the document. Since there are numerous different nickel compounds it is not possible to give CAS and EC numbers on the front page of this document. |
| **RAC Rapporteurs comments**  Thank you for your comment. |

1. Regarding the term “mode of action-based threshold” see Joint Task Force ECHA Committee for Risk Assessment (RAC) and Scientific Committee on Occupational Exposure Limits (SCOEL) on Scientific aspects and methodologies related to the exposure of chemicals at the workplace. Task 2. 6 December 2017. https://echa.europa.eu/documents/10162/13579/jtf\_opinion\_task\_2\_en.pdf/db8a9a3a-4aa7-601b-bb53-81a5eef93145 [↑](#footnote-ref-1)