EXPLANATORY MEMORANDUM

1) BACKGROUND TO THE PROPOSAL

1.1) Reasons for and objectives of the proposal

This proposal adapts Annex I to Council Directive 67/548/EEC[1] to technical progress, as foreseen under Article 28 of that Directive. This is the thirty first time that the Annexes to Directive 67/548 are being adapted to technical progress.

The Directive places an obligation on the Commission to make proposals for harmonised classification and labelling of substances, by amending Annex I, placing priority on substances having carcinogenic, mutagenic and reproductive toxic effects. This proposal includes a number of substances newly identified as having carcinogenic, mutagenic or reproductive toxic effects.

The Annex also needs to be revised if new scientific evidence shows that entries in Annex I are no longer correct.

The objective of this proposal is therefore:

(1) to add substances which are not yet in Annex I, due in particular to their carcinogenic, mutagenic or reproductive toxic effects, which should be placed in Annex I with urgency;

(2) to revise the classification and labelling of substances listed in Annex I based on new scientific evidence,

with a view to ensuring that the information on the effects of these substances is communicated to all users, enabling them to take the appropriate precautionary measures.

1.2) The Global Context

The hazard classification under the newly approved Globally Harmonised System for classification and labelling is consistent with the application of the specific classification criteria in Section 4 of Annex VI to the Directive. The continued efforts of the EU to adapt Annex I to technical progress, in particular for substances with carcinogenic, mutagenic and reproductive toxic effects, is therefore fully in line with the EU's commitment to implement the globally harmonised system for classification and labelling.

1.3) The EU Context

The classification and labelling part of Directive 67/548/EEC places an obligation on suppliers of dangerous substances to carry out investigation to make themselves aware of the relevant and accessible data which exists concerning the properties of their substances. On the basis of this information, they shall label and package their substances accordingly. The obligation to self label and package substances applies until a harmonised classification has been adopted through an adaptation to technical progress of Annex I.

[1] hereafter referred to as the Directive

The Commission has a particular obligation to act swiftly for substances with carcinogenic, mutagenic or reproductive toxic effects.

1.4) Coherence with other policies

Several pieces of Community legislation refer to the classification criteria in Annex VI to the Directive or to the actual listing of substances in Annex I, for which classification is harmonised. This Community legislation relies on the Directive to provide information on the dangerous properties of substances. The Directive and these other pieces of Community legislation form a coherent system of policies, designed to protect humans and the environment.

This proposal ensures that the information necessary for users of the substances included in the proposal is provided allowing users to take the appropriate precautionary and first aid measures.

2) LEGAL ELEMENTS OF THE PROPOSAL

Proportionality

The criteria for the classification of substances as dangerous have been developed and agreed based on previous amendments and adaptations to technical progress. Other Community legislation, which refers to the Directive, has been adopted having the consequences of the classification of substances carried out under the Directive in mind. The main purpose of the Directive is to provide for information on hazardous properties of substances to be communicated to all users, enabling them to take the appropriate precautionary measures. This proposal enables the harmonised provision of hazard information for the substances covered by the proposal.

The fact that some compounds were classified and not all shows that proportionality, as well as necessity, have been taken into account in the drafting process. Also, the fact that some endpoints were classified for some compounds, but not all, also proofs that the Directive was drafted with the objective of ensuring that the proposed measures is the least trade restrictive measure available to fulfil the legitimate objective of protecting health and safety, and is therefore compatible with Article 2.2 of the TBT Agreement.

Therefore this proposal for a Directive is proportionate.

3) DOWNSTREAM CONSEQUENCE OF THE PROPOSAL

As regards downstream consequences of this classification, it has to be noted that a large number of EU Directives and Regulations (e.g., Directive 99/45/EC concerning the approximation of the laws, regulations and administrative provisions of the Member States relating to the classification, packaging and labelling of dangerous preparations, Directive 96/82/EEC on the control of major-accident hazards involving dangerous substances, Directive 91/689/EEC on hazardous waste, Directive 98/24/EC on the protection of the health and safety of workers from the risks related to chemical agents at work, Directive 2004/37/EC on the protection of workers from the risks related to exposure to carcinogens or mutagens at work, Directive 76/768/EEC on the approximation of the laws of the Member States relating to cosmetic products, Directive 98/8/EC concerning the placing of biocidal products on the

market, Directive 91/414/EEC concerning the placing of plant protection products on the market, see: http://ecb.jrc.ec.europa.eu/documents/Classification-Labelling/3199r5_ECB_Downstream_legislation.doc), include specific obligations if the substance in question is classified in accordance to Directive 67/548/EEC. Two Directives are of particular relevance, in this respect, since they trigger examinations on the need for marketing and use restrictions in case of a classification of a substance CMR cat.1 or Cat. 2

- Directive 76/769/EEC on the approximation of the laws, regulations and administrative provisions of the Member States relating to restrictions on the marketing and use of certain dangerous substances and preparations obliges the European Commission to consider if a ban or restrictions are necessary for such substances used as such or in preparations with consumer use.

- Directive 76/768/EEC on the approximation of the laws of the Member States relating to cosmetic products provides for a ban of those classified substances in cosmetic products above certain concentration levels.

Industry and some third countries have argued that the classification would have serious consequences under REACH, in particular, that all such compounds would have to be authorised. Under Regulation (EC) No 1907/2006 on Registration, Evaluation, Authorisation and Restrictions of Chemicals (REACH), substances classified as CMR category 1 or 2 will indeed be potential candidates for authorisation. However, it is important to note that the authorisation requirement applies neither directly nor automatically. The process of identifying substances to be subject to authorisation consists of two steps (the establishment of the candidate status of the substance and then, the prioritisation of the substance for the actual authorisation procedure) which are subject to scientific evaluations following transparent scientific procedures. If a substance meets the criteria for classification as carcinogenic, mutagenic or toxic to reproduction category 1 or 2 (CMRs) in accordance with Directive 67/548/EEC, the step to identify the intrinsic properties may be limited, if appropriate, to a reference to an entry in Annex I of Directive 67/548/EEC. In addition, REACH provides for the possibility of exemptions to the obligation to obtain authorisations for certain uses or categories of uses. Authorisation will be given either on the basis of adequate control of the risks, or on the basis of a socio-economic analysis proving that the benefits from the substance's use outweigh the risks it poses to human health or the environment and that there are no suitable alternative substances or technologies..

4) INTRODUCTION TO THE PROPOSAL

In developing its proposal for adaptations to technical progress, the Commission consults the Technical Committee on Classification and Labelling composed of experts appointed by the Member State Competent Authorities responsible for the implementation of the Directive. The Commission may also, when appropriate, consult specialised experts, designated by the Member States and having special qualifications with respect to either carcinogenicity, mutagenicity or reproductive toxicity, for the purpose of obtaining specialised advice. This proposal is based on the recommendations of the Technical Committee on Classification and Labelling and in some cases the advice given by the specialised experts.

The 31st ATP to Directive 67/548/EEC contains a large number of substances classified for carcinogenicity, mutagenicity or reproductive toxicity. The classifications of 22 existing entries have been revised to include these effects. In addition, 96 entries with these effects are

included in the Annex for the first time along with another 110 new entries for substances that may cause either sensitisation by inhalation and skin contact or serious damage to health from prolonged exposure. This information will allow manufacturers, importers and downstream users of these substances to apply, or recommend, risk reduction measures to protect workers, the general public and the environment in a harmonised way from these effects.

The above changes are contained in three annexes to the draft directive:

Annex 1 A: Revised C&L for existing entries => 83 entries (6 on nickels covering 12 out of 100 substances)

Annex 1 B: C&L for new entries => 385 entries (45 entries on Nickels covering 118 out of 500 substances)

Annex 1 C: Deleted entries => 4 entries

Due to their commercial importance and sustained activities of the nickel industry, the proposed classification of some 130 nickel compounds has attracted particular attention and this paper therefore aims in particular to explain the history of and scientific rationale for the proposed classifications.

5) THE PROPOSAL FOR CLASSIFYING NICKEL COMPOUNDS

Procedure for harmonised classification:

The determination of the classification of a substance requires specialised knowledge about the intrinsic properties of the substance. In order to provide a solid scientific basis for the preparation of Commission proposals for harmonised classification and labelling, DG Environment has set up a committee of Member State experts and industry observers, called the Technical Committee on Classification and Labelling (TC C&L). Meetings of this Technical Committee are organised by the European Chemicals Bureau (ECB) at the Commission's Joint Research Centre (JRC) Ispra. All conclusions the TC C&L arrives at are recommendations for possible inclusion in an ATP of Directive 67/548/EEC.

Category/Grouping approach:

The category or grouping approach is a technique for grouping closely related chemicals that are then considered as a category, or group, rather than individual chemicals. Under this approach, not every chemical needs to be tested for every effect. The overall data set allows the estimation of the hazard for the untested endpoints for the chemicals in the category. The structural similarities may be based on a common functional group (acid, alcohol, specific metal ion). The category approach[2] is explicitly listed in Annex XI of REACH as an alternative method to avoid animal testing. The OECD has also published a detailed guidance on the grouping of chemicals into categories. The OECD guidance document is based on the guidance developed by US Environmental Protection Agency, the experience gained within the EU on classification and labeling and on risk assessment and the experience gained within OECD program on chemicals.

[2] The terms category and grouping have the same meaning. In the present reply, the EC consistently uses the term category and category approach.

The category approach is widely used in Annex I (list of classified dangerous substances) to Directive 67/548/EEC with its first application in the 15th ATP. Nearly 100 group entries are already included in Annex I covering a number of metals and their compounds, petroleum streams and gasses, but also organic groups such as chloroanilines or chloronitroanilines.

The approach adopted when evaluating the classification of the entries covering metals and their compounds was the conclusion that it was the metal ion which was the main determinant for the chemical inherent properties of the substance.

These entries took the form of group entries, where a specific classification was allocated to all substances containing the metal. In the cases where data was available to justify specific deviations from the general rule for a specific substance, specific entries where listed. As an example, the 29th ATP added the environment classification to the lead entry:

Annex I entry number: 082-001-00-6

lead compounds with the exception of those specified elsewhere in this Annex

Risk Phrases: R: 61-20/22-33-62-50/53

Elsewhere in Annex I, a specific entry for example for lead azide has the following listing:

Annex I entry number: 082-003-00-7

lead azide

Risk Phrases: R: 61-3-20/22-33-62-50/53

Where the additional classification as explosive (R3) was added. The general lead entry could cover up to as many as 400[3] lead compounds and a similar entry for chromium (VI) compounds could cover up to as many as 50[3].

This approach has been applied not only to metals and their compounds, but also to other substances (e.g., chloroanilines, Annex I entry number 612-010-00-8 or salts and esters of MCPA, Annex I entry number 607-052-00-9). Based on a proposal by CONCAWE a category approach was applied to identify which of the approximately 500 different UVCB substances (substances of Unknown or Variable composition, Complex reaction products or Biological materials) covering most petroleum streams and gases require classification for carcinogenicity and which would not require such classification.

Classification History and Scientific rationale for classification of Nickel compounds

History of Nickel compounds classification:

The Danish EPA has reviewed five selected nickel compounds under Regulation (EC) N° 793/93 (the EU existing chemicals programme). They applied a category approach to the five substances nickel (metal), nickel sulfate, nickel dichloride, nickel dinitrate and nickel

[3] This is the approximate number of compounds found in EINECS, which does not necessarily reflect the substances which are on the market today.

carbonate. In accordance with Annexes I, II and III of Regulation (EC) N° 1488/94 (the Risk Assessment Regulation established in accordance with Article 10(4) of Regulation (EC) N° 793/93) the risk assessment of the five substances include a review of the classification and labelling of the substances. The conclusions of the human health part of the 5 risk assessments were endorsed by the Commissions' SCHER (Scientific Committee for Health and Environmental Risks). As a consequence of this review, the Commission in the 30th ATP saw the need to amend Annex I to revise the classification of these five substances.

In applying the category approach to the five substances subject to risk assessment under Regulation (EC) N° 793/93, the Danish EPA collected and evaluated data on a total of 12 nickel compounds (including the five risk assessment substances)..

The 30th ATP only revised the classification of five of the existing nickel entries. As a support to the risk assessment of the 5 nickel substances, data was also collected on 7 more nickel compounds leading to revised classification proposals by the Danish EPA. Given that a large number of other nickel compounds are not covered by Annex I and given the obligation manifested in Annex VI, paragraph 4.1.5 of Directive 67/548/EEC, to act as soon as possible if a substance is expected to be a carcinogen, in 2005 the Danish EPA also considered that additional proposals for classification of relevant other nickel compounds based on a category approach were necessary.

Identifying as many nickel compounds as scientifically justifiable[4] having or lacking carcinogenic (or other) properties also helps reduce market disruptions. If only some nickel compounds are included in Annex I as Category 1 carcinogens this might lead to market distortions, since if nickel compounds with similar properties are not included in Annex I, they could be perceived to be safer than those with a harmonised classification, and lead to unjustified substitution of nickel compounds currently in use by others not included in Annex I. This argument was one of the reasons for classifying the approximately 500 individual petroleum streams and gasses using a category approach in the 21st ATP.

There are a number of scientific reasons underlying any grouping of nickel compounds for estimating their biological properties. The main basis is that it is the nickel ion that is responsible for the effects to be assessed. The concentration of the ion at the site of action is the most important factor determining the toxicity of the compound, however this information is normally not known and in any case difficult to determine experimentally. Bioavailability can be used as tool to establish categories. Simply defined, bioavailability is the fraction of the metal ion that reaches target sites for toxicity. The bioavailability depends on various characteristics of the individual nickel compounds of which solubility in water is considered as being particularly important for the release of the nickel ion and has therefore been used as an approximation of systemic bioavailability of the nickel ion.

Using water solubility as a (initial) criteria to define the category is therefore based on the argument that nickel substances having similar water solubility will induce similar bioavalability of the Ni(2+) ion. This observation in itself would not be sufficient to apply a read across though. Sufficient information regarding the effect under consideration needs to be available for the substances from which the read across is applied to fill data gaps.

[4] A classification can only be made if positive information exists fulfilling the criteria. If no information exists for an effect or if insufficient information is available to justify fulfilment of the criteria for that effect then it is not possible to classify the substance for that effect.

The division into groups across the spectrum of water solubility follows the approach already widely used for nickel compounds[5] (see also the background document used in the risk assessments of the five substances assessed under Regulation 793/93) and indeed applied to other metal compounds as well. Water solubility is thereby an acceptable measure of similarity between nickel compounds. The read-across[6] within groups and between groups of compounds of similar water solubility is not only justified, but provides the possibility of hazard identification that would be difficult for certain endpoints or would involve the use of costly animal testing and thus the unnecessary use of experimental animals.

The importance of water solubility and indeed of other factors contributing to toxicity varies depending on the type of toxic effect under consideration. In the category approach applied to the nickel compounds, the importance of water solubility and of the other factors are evaluated and validated for each group of substances based on the available mechanistic and toxicity information. Where the evaluation of the effects of the nickel compounds in a specific group lead to the conclusion that the read across with in the group could not be applied, no classification was proposed for that effect and group.

Starting from the broadest possible characterisation of the category "nickel and nickel compounds", there are more than 300 identified compounds listed in EINECS (European INventory of Existing Commercial chemical Substances) alone having a very diverse chemical structure. In addition, there is a vast database on the human health effects of nickel compounds. However, the data available for any individual nickel compound can vary considerably. The two compounds for which there is data that covers most endpoints are the two soluble compounds, nickel dichloride and nickel sulfate. Much of the database relating to nickel metal is linked to sensitisation. On the other hand, there is very limited data available for most other nickel compounds. In particular, data on the organic nickel compounds is very limited.

Due to lack of data for many Nickel compounds a category approach was proposed by the Danish EPA[7]. A matrix was elaborated on the data availability on selected nickel compounds. A sufficiently good dataset exists for some of the water soluble and the insoluble compounds to develop a category approach and use read-across to interpolate to substances with less data. The group of slightly soluble salts is the group with the least data. However, it is positioned in the middle of the solubility range of the group of more data rich compounds of greater and less solubility. Due to this positioning it is possible to compensate for lack of data, at least to some extent, by applying read across.

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[5] The NiPERA report prepared for DG V in 1996 (Occupational exposure limits: Criteria Document for nickel and nickel compounds. Volume I: Summary, Conclusions and Recommendations; Volume II: Assessment of Occupational Exposures; Volume III: Health Assessment of various species of Nickel. Prepared by NiPERA in collaboration with Eurométaux for the European Commission, Directorate General V. Public health and Safety at Work Directorate. Batiment Jean Monnet, Plateau du Kirchberg. L-2920 Luxembourg) considers compounds under the headings of "soluble nickel", "sulphidic nickel", "oxidic nickel", "metallic nickel" and "nickel carbonyl". Other reviews, such as the TERA (1999) (Toxicological review of soluble nickel salts. Prepared for: Metal Finishing Association of Southern California, Inc., US Environmental Protection Agency and Health Canada.) base their conclusion on a common biological effect across a range of water solubilites.

[6] Read-across approach: Human health and environmental effects may be predicted from data for reference substances by interpolation to other substances in the group.

[7] See http://cms.mim.dk/NR/rdonlyres/07DB028E-134E-4796-BF6D-97B9AD5F9E82/0/Nikkel.pdf

Article 4(3) of Directive 67/548/EEC stipulates that the harmonised classification of substances in Annex I should be as complete as the available information enables, meaning that an active decision should be taken whether to classify or not for each effect for which information is available. Based on this obligation the DK EPA developed a category approach and applied read across to all classification end-points in their original proposal, with the aim to have a discussion and decision as to which effects a classification decision was possible, leading to the decision to classify or not based on sufficient available information, and for which effects the available information is insufficient to justify classification, leading to the decision not to classify based on the fact that insufficient information was available to take a decision. This approach is also scientifically justifiable.

In November 2005 there was a wide-ranging discussion in the TC C&L of the principle and detail of the proposal. Member States were willing to accept the concept of a group approach, but concluded that further detailed discussion was needed on specific issues. For a number of end points (acute toxicity, irritation) it seemed, not surprisingly, that other factors, such as the non nickel part of the substance and the counter ion had significant impact on the toxicity for those substances where data was available. In addition industry also signaled concern that water solubility was not an appropriate indicator of toxicity.

In **March 2006** a modified and reduced proposal from Denmark was discussed. There was Member State consensus towards agreement on a reduced number of substances (e.g.., exclusion of metal-metal substances) and a reduced number of end points. However fundamental differences of opinion with the nickel industry remained. The representatives of the Industry made clear they did not regard the proposal as scientifically valid and also that they regarded the proposal as not applying the criteria for classification in Annex VCI of the Directive. In the Nickel industry's view the Directive calls for specific substance-based information. Member State did not regard these concerns as grounds for invalidating the modified proposal. Indeed several argued that the work was a clear priority and should progress in order to be concluded as part of the 31st ATP.

The discussion concluded with Member States' agreement to a written procedure for the final refinement of the proposal based on discussions in the meeting. No Member State opposed the final proposal.

In December 2007, the recommendation from the Member States was placed on the ECB website.

On 29 September 2008, the Commission organised a working group meeting of the Technical Progress Committee of Directive 67/548/EEC. The main objective of the meeting was to give the Commission an opportunity to consult the Working Group and obtain its views regarding the classification of Nickel compounds as proposed in the draft of the 31st ATP, by taking into account new information provided by the Nickel Industry and the review of the category approach applied for the Nickel compounds classification performed by the Australian National Industrial Chemicals Notification and Assessment Scheme (NICNAS). The expert from NICNAS emphasized that even if read-across within subgroups is acceptable; the reading-across between subgroups is questionable. In particular, due to insufficient data on the slightly soluble compounds, it is difficult to predict whether these compounds would behave as soluble or insoluble compounds. She emphasized that several factors (e.g., chemical structure, particle size, solubility, bioavailability) need to be taken into account to estimate the behaviour of slightly soluble compounds and that water solubility should not be the main determinant to base the read-across on. She underlines that the mode of action for

carcinogenicity for soluble and insoluble Nickel compounds is different. She concluded by saying that data on the extent of the release of the nickel ion from the nickel compounds in the biologically relevant media would help to determine which groups are similar. Experts from Member States explained the rationale of this approach as described below in sections "*Rationale for the category approach"* and *"Rationale for each endpoint retained in the category approach".*

The representatives from Nickel Industry stated that water solubility is not an appropriate nickel compound grouping criteria for read-across as:

- no compound specific water solubility data are provided in the proposal,

- water solubility does not predict any of the toxicity endpoint for which data exists,

- no verification of the validity of the water solubility based read-across was performed,

- all the data which are available to date disprove the veracity of using water solubility based read-across for nickel compounds,

- no data support the water solubility grouping paradigm.

Therefore, Nickel Industry suggested that a better option (e.g., bioaccessibility approach) should be followed.

Several experts from Member states questioned the validity of the approach proposed by the Nickel Institute and expressed some doubt about its relevance and the interpretation of the results especially for chronic endpoints like carcinogenicity. Furthermore, some experts expressed concern for the introduction of an extensive testing regime including *in vivo* testing and questioned whether this new approach had gained broad acceptance within Industry in general. The working group concluded that it is not necessary to wait for the bioaccessibility information that should be submitted by Nickel Industry in the coming months and the 31st ATP proposal of the Commission should go forward.

Information submitted by Industry:

The nickel industry was mainly represented in the meeting of the TC C&L by Eurométaux, and included ENiG (the European Nickel Group), ENIA (European Nickel Industry Association) and NiPERA (the US based Nickel Producers Environmental Research Association). ENIA is the European branch of the Nickel Institute, which itself has also taken part in the discussions.

The nickel industry, while agreeing to apply the principle of read across when clear rules like those developed by the OECD would be applied and expressing themselves a concern[8] for possible carcinogenic effects (leading eventually to a category 3 classification) of all nickel compounds, considered this approach to be subject to validation. The Nickel industry argued that the approach using water solubility is scientifically invalid as it assumes the mechanism relies on the nickel ion alone and ignores delivery mechanisms. Since 2005 the Nickel Institute has sent several letters to the Commission claiming that the 31st ATP is based on flawed science. They also provided the Commission with the view of an expert panel that supported the nickel industry's conclusions. However, the nickel industry has as yet not submitted any information or experimental results on the basis of which members of the TC

[8] Notwithstanding the recognition of concern, the nickel industry clearly objected to classification in Categories 1 and 2 for most nickel compounds.

C&L were ready to change their original opinion on the hazardous properties of the Nickel compounds at stake.

Industry has had the opportunity to put forward data disproving this classification. One branch of Industry, Eurocolour, a CEFIC sector group, has taken advantage of this possibility in close collaboration with the Danish representatives in the TC C&L. This has led to the deletion of a number of pigments containing nickel compounds from the proposal, as the data generated by the CEFIC sector group showed that the application of the group assessment approach to some pigments was not justified. The certain nickel pigments were not excluded on the basis that their water solubility was proved wrong. They were excluded because the crystal structure of these compounds was sufficiently different from that of the comparison compounds (nickel oxides) to invalidate the comparison. When nickel release from these different structures was measured it was demonstrated to be significantly different to the comparison compounds and hence demonstrating that the structures of these substances was so different from the comparison compounds that read across could not be justified. Both the nickel industry and other Industry groups are not prevented from carrying out further testing after a classification has been made, if it considers that the data derived from such testing can demonstrate that the classification should be changed.

Classification of the Ni compounds in the 31st ATP proposal:

For the purposes of this evaluation, nickel compounds are placed in one of eight sub-categories:

a) nickel sulfate, nickel dichloride, nickel dinitrate and other soluble compounds with a water-solubility greater than 10^{-2} mol/L (groups of "soluble" compounds).
Classification: Carcinogen cat. 1, reproductive toxicant cat.2, Mutagen cat. 3, chronic toxicity by inhalation, sensitisation by inhalation and skin contact, very toxic for the environment.

b) nickel carbonate, nickel dihydroxide and other slightly soluble compounds with a water-solubility in the range 10-4 -10-2 mol/L, (group of "slightly soluble" compounds).
Classification: Carcinogen cat. 1, chronic toxicity by inhalation, sensitisation by inhalation and skin contact, very toxic for the environment.

Note: The known oral uptake of nickel carbonate and nickel dihydroxide has been used to justify the inclusion of classification of these substances for systemic effects, but has not been used to include this classification for other nickel compounds of a similar water solubility.

c) nickel sulphide, nickel subsulphide and other 'insoluble' compounds with a water solubility less than 10-4 mol/L (group of "insoluble" compounds)
Classification: Carcinogen cat. 1, chronic toxicity by inhalation, sensitisation by skin contact, very toxic for the environment.

d) nickel oxide and mixed nickel oxides
Classification: Carcinogen cat. 1, chronic toxicity by inhalation, sensitisation by skin contact, possible of long term effects for the environment.

e) metallic nickel and metallic nickel compounds

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Not included. Studies on the inhalational carcinogenicity of metallic nickel are currently in progress, and the relevance of including these metal-metal compounds can be considered when the results of this study have been evaluated.

f) nickel carbonyl

No change to the current classification.

g) nickel compounds specifically excluded from the category; see: <http://cms.mim.dk/NR/rdonlyres/07DB028E-134E-4796-BF6D-97B9AD5F9E82/0/Nikkel.pdf >

h) nickel compounds not included in the category; see: <http://cms.mim.dk/NR/rdonlyres/07DB028E-134E-4796-BF6D-97B9AD5F9E82/0/Nikkel.pdf >

Rationale for the category approach:

The category approach used starts by grouping nickel compounds in a number of subcategories on the basis of their water solubility. Read-across is then carried out within each of these subcategories on the basis of the agreed hazards of individual substances in each subcategory. The essential refinement of the approach was to remove from each group compounds that would not be expected to behave similarly to the nickel compound used for comparison. Such behavioural dissimilarity can be based on mechanistic differences (or uncertainty about the mechanistic similarity), differences in chemical composition, complexity or geometry or other differences.

For instance:

1. Compounds known to be nickel(I) compounds have been excluded as the approach is based on the toxicity of the nickel(II) ion.

2. Nickelates have been systematically excluded due to their specific structural properties differing significantly from nickel oxide and the lack of data on which to assess the validity of any potential read-across from the other nickel compounds for which data is available.

3. Tetraammine and hexaammine compounds have also been excluded as the read-across from the hexaammine nickel complex to a hydrated nickel ion is not necessarily appropriate.

4. Studies have shown a different pattern of nickel release from the spinels, rutiles, periclase to bunsenite compared to nickel oxide, and this justifies the exclusion of these compounds from the category.

5. Nickel forms metal-metal compounds with a number of elements. These compounds are substances and not alloys, and the compounds with aluminium, niobium, lanthanum, dysprosium and bismuth are known to be on the market. The classification of metallic metal has been based on data for the compound and not on read-across from any of the other nickel compounds under review. In particular, the classification for cancer has been based on the limited data available rather than on read-across. Studies on the inhalational carcinogenicity of metallic nickel are currently in progress, and the relevance of including these metal-metal compounds can be considered when the results of this study have been evaluated.

6. There are a number of nickel containing compounds on the market listed as high production volume chemicals or, in some cases, as low production volume chemicals, which are not considered as relevant for consideration in a category approach, as their effects are not considered to be adequately described by their nickel content. Examples are Asphalt (EC No: 232-490-9, CAS No. 8052-42-4), "Glass, oxide" (EC No: 266-046-0, CAS No: 65997-17-3) and "Ceramic materials and wares" (EC No: 266-340-9, CAS No: 66402-68-4) "Frits, chemicals" (EC No.: 266-047-6, CAS No.: 65997-18-4), Copper matte (EC No.: 266-967-8, CAS No.: 67711-91-5), Copper smelting slags (EC No.: 266-968-3, CAS No.: 67711-92-6) Ashes (residues) (EC No.: 268-627-4, CAS No.: 68131-74-8) Lead alloy, base, Pb, Sn, dross (EC No.: 273-701-4, CAS No.: 69011-60-5) Waste solids, copper electrolyte purifn. cathodes (EC No.: 273-720-8, CAS No.: 69012-20-0) Leach residues, zinc ore-calcine, cadmium-copper ppt. (EC No.: 293-311-8, CAS No.: 91053-46-2) Leach residues, zinc ore-calcine, iron-contg. (EC No.: 293-312-3, CAS No.: 91053-47-3) ferro-nickel slags (EC No.: 273-729-7, CAS No.: 69012-29-9)

7. Seven nickel compounds were deleted because of the presence of a double bond which makes the molecule more likely to be biologically active. However, this property is significantly different than the nickel compounds used for comparison and so the read across can not be justified.

8. For 5 nickel compounds it was considered that organic moiety would contribute significantly of the to the overall hazard profile. As this was not present in the nickel compounds used for comparison, no read across could be carried out. However, a category of these compounds could be considered as such.

9. There was uncertainty about the identity of one nickel compound (nickel metaborate) and therefore it was excluded from the category.

The approach recognises that water solubility is a predictor for systemic bioavailability of nickel but not necessarily for bioavailability in lung tissue where specific up-take mechanism may operate. Information on bioavailability has been taken into account where this is available. This type of information is not normally available when making proposals for group classifications for Annex I. Thus historically in some cases no distinctions have been made (e.g. all lead metal compounds are given the same classification in Annex I, an approach apply also by lead industry in their voluntary risk assessment carried out in consultation with the experts working under Regulation (EC) N° 793/93); in other cases individually named compounds have been excluded, largely based on the water (in)solubility.

For each toxicological end-point a specific decision was made whether read-across could be justified. This has lead to the exclusion of certain end-points from the read-across in the different groups of water solubility

Rationale for each endpoint retained in the category approach:

Carcinogen category 1: There is epidemiological evidence for carcinogenicity of some soluble nickel compounds as well as of some insoluble soluble and nickel oxides. Chronic animal studies have shown carcinogenicity for the poorly water-soluble nickel compounds tested.

The overall findings indicate that nickel ions generated in target cells are critical determinants for the carcinogenic process.

The cellular uptake of soluble and insoluble nickel compounds is different as insoluble nickel compounds enter the cell via phagocytosis[9], while soluble nickel compounds enter the cell via metal ion transport systems or through membrane diffusion. The latter two processes are much less efficient implicating that the same extracellular levels of soluble and insoluble nickel compounds lead to lower intracellular nickel levels for soluble nickel compounds. Soluble forms of nickel interact with the cell in a way that maximises cytotoxicity and minimises nickel delivery to the nucleus and interaction with DNA, while insoluble forms of nickel interact with cells in a way that decreases the cytotoxic potential while increasing the delivery of nickel to the nucleus. Thus, the mechanism for cellular uptake could differ between soluble Nickel compounds and insoluble ones. For the group of "slightly soluble" compounds, the mechanism for cellular uptake is unknown and could be similar either to the one of the soluble nickel compounds or to the one of the insoluble nickel compounds. However, since both groups are classified as carcinogens, the group of "slightly soluble" should also be classified in a similar way. This has been evaluated and agreed by e.g. the Specialised Experts consulted on the classification of nickel carbonate in the context of the TC C&L, the SCHER through its opinion on the nickel risk assessment reports, and the OECD SIAM, in its review of the SIAPs for the five nickel compounds reviewed under the EU ESR programme and it is the logic followed for the 30th ATP in which the soluble and slightly soluble compounds listed in the ATP have been classified as carcinogens. Indeed, it is reasonable to assume that all nickel compounds that can create nickel ions inside or outside the cell are carcinogenic to humans following exposure by inhalation. As a consequence, soluble, slightly and insoluble Nickel compounds as well as nickel oxides are proposed to be classified as carcinogens in the 31st ATP.

Chronic toxicity by inhalation: Inhalation of the insoluble nickel compounds (subsulphide and oxide) results in lung inflammation and fibrosis. Inhalation of the soluble nickel sulphate and chloride also affects the lungs. Chronic lung inflammation and lung fibrosis are serious and potentially irreversible effects. Repeated dose toxicity following inhalation is an effect that leads to classification of both soluble (nickel sulphate) and insoluble nickel compounds (nickel subsulphide and nickel oxide). The effects are seen at substantially lower levels with nickel sulphate than with the insoluble compounds. For this effect, we are in the same situation as for carcinogenicity, therefore, a logic similar to carcinogenicity is followed. In other words, soluble, slightly and insoluble Nickel compounds as well as nickel oxides are proposed to be classified as toxic by inhalation following repeated exposure in the 31st ATP.

Reproductive toxicity category 2: There are no relevant studies in humans. Only animal data on two soluble nickel compounds are available. In the 30th ATP, based on the consistent evidence of developmental toxicity (stillbirth, post-implantation/perinatal lethality) in rats at dose levels not causing maternal toxicity, some soluble nickel compounds have been classified for developmental toxicity in Category 2. As the available information is limited to soluble nickel compounds, where systemic effects have been demonstrated in the comparison compounds, it is proposed in the 31st ATP to use read across for the group of soluble nickel compounds as reproductive toxicant.

[9] A cellular process whereby the cell engulfs solid particles by cell membrane to form an internal membrane-bound compartment.

Mutagen category 3: There is considerable evidence of the *in vitro* genotoxicity of nickel compounds. Positive effects are generally seen in studies of chromosomal effects, cell transformation tests and tests for DNA damage and repair. Interpretation of the results of *in vivo* studies is more complicated. Most of the studies have been carried out with the three soluble nickel compounds listed in the 30th ATP. There is little *in vivo* data on other soluble compounds, and data on slightly soluble nickel compounds and insoluble compounds is also very limited. In the 30th ATP, based on the evidence of in vivo genotoxicity in somatic cells, after systemic exposure, some soluble nickel compounds have been classified as mutagens category 3, as the possibility of systemic effects on the germ cells cannot be excluded. As the available information demonstrates mutagenicity only for soluble nickel compounds, it is proposed in the 31st ATP to use read-across for the group of soluble nickel compounds as mutagens category 3[10].

Sensitisation by skin contact: Nickel is well known as a skin sensitizer, and is one of the most frequent skin sensitizers in man. Nickel skin sensitisation has been evaluated almost entirely on the basis of human studies with very water-soluble nickel compounds, and studies on release rates with nickel metal. There is limited data on skin sensitisation or nickel release from compounds with lower water-solubility. There is however agreement that this effect also occurs with compounds with very low water solubility such as nickel oxide. In a similar way as for carcinogenicity and Chronic toxicity by inhalation, soluble, slightly and insoluble Nickel compounds as well as nickel oxides are proposed to be classified as sensitizers by skin contact in the 31st ATP.

Sensitisation by inhalation: Respiratory sensitisation is recognised as an effect with the soluble and slightly water-soluble nickel compounds. The TC C&L has agreed that (insoluble) nickel sulphide, nickel subsulphide or metallic nickel should not be classified for this end-point, although there is limited evidence from people exposed to metallic nickel, and some suggestion that this effect can also be seen with other compounds, as shown by the anecdotal evidence that nickel matte also shows this effect. The TC C&L agreed to read-across this classification for all the soluble and slightly soluble nickel compounds. It is possible that further studies may show that this effect occurs across a wider spectrum of water-solubility than is currently recognised.

Toxicity for the environment: Metal compounds may be toxic in the aquatic environment depending on the toxicity of the metal ion and the rate and extent to which metal compounds can produce soluble available ionic species in aqueous media. The availability of a metal substance means the extent to which the metal ion portion of a metal compound can disaggregate from the rest of the compound. To determine the classification of a nickel substance, its capacity to solubilise in water and liberate its nickel ion is compared with the reference toxic value for the nickel ion. The appropriate $L(E)C_{50}$ value for the evaluation of Nickel compounds is 0.068 mg/L. On the basis of this analysis, all the nickel compounds with the exception of the nickel oxides and metallic nickel should be classified as very toxic for aquatic organisms.

Rationale for each endpoint excluded from the category approach:

[10] Nickel carbonate and nickel hydroxide are also classified for this effect as there is evidence of systemic uptake for these compounds.

Irritation/corrosivity: The available data that indicates that soluble nickel compounds can cause skin irritation is derived from humans, whilst the available animal data does not support classification for this effect. Unlike nickel sulphate, nickel dinitrate showed severe eye irritation. It was suggested that the greater severity of this compound was due to its oxidising properties. This suggests that this local property is more dependent on the counter ion[11] than other systemic effects. This endpoint not only depends on the water solubility of the nickel compound, but also on the nature of the anion[12], and that the read-across for nickel salts must include an evaluation of not just nickel ion availability, but also the irritancy of the anions. Since the water soluble nickel salts are not irritating at concentrations below 20% it will be difficult to consider a direct extrapolation of irritancy data without some knowledge of the bioavailable fraction of nickel released by a particular compound and the potential irritancy of the molecule to which it is bound. Therefore in conclusion, the available information is not sufficient to validate the category for irritation and corrosivity and apply read across to the substances with no available data.

Acute toxicity: Most of the available data for both soluble and slightly soluble compounds is in the range of oral toxicity covered by the criteria for "harmful". The counter ions may lead to increased toxicity, and it is likely that there are additional soluble nickel compounds that, like nickel chloride, show a toxicity in the range of oral toxicity covered by the criteria for "toxic" or "very toxic". Though it is evident from the available information that soluble and slightly soluble nickel compounds are at least “harmful”, the available information for the substances with high toxicity is not sufficient to allow an understanding of the important additional factors driving the additional toxicity enabling the application of read across to all the substances in the category.

6) MAIN CONCERNS OF THIRD COUNTRIES AS EXPRESSED IN THE WTO-TBT CONTEXT

*** Technical/Scientific concerns**

- *The classification of nickel compounds set a negative precedent for regulating others mineral and substances under REACH.*

Commission answer: The EC confirms that the nickel group classification does not provide a model to be used directly for other groups of chemicals as every grouping should be done on a case by case approach. The category approach is explicitly listed in Annex XI of REACH, with the strong support from Industry, as an alternative method to avoid animal testing.

- *The classification of nickel compounds is not transparent (e.g, expert judgement should be provided), is not scientifically justified and is not based on sound scientific principles and on a robust approach.*

Commission answer: A comprehensive explanatory note has been provided with the notification of the 31st ATP proposal. This note explained in detail the classification history and scientific rationale for classification of Nickel compounds (see chapter 5 of the explanatory memorandum). In addition, the Commission organised a specific expert meeting

[11] The ion that accompanies an ionic species in order to maintain electric neutrality.
[12] A negatively charged ion, which has more electrons in its electron shells than it has protons in its nuclei.

to reply to any technical questions WTO countries could have. With regards to the relevant scientific information, the EC would like to point out that all the information used by the experts of the Technical Committee on Classification and Labelling (TC C&L) is publicly available. It can be downloaded from the following website: http://ecb.jrc.ec.europa.eu/classification-labelling/ under "Documents" and in the folder called "BACKGROUND DOCUMENTATION TO NICKEL-ENTRIES IN ATP 31" This scientific information provided the EC with sufficient evidence to enable the application of the Criteria in Annex VI.

- *The classification of nickel compounds relies only on water solubility, that is not a predictor of the solubility in biological fluids and that is no available for most of the Nickel compounds listed in the 31st ATP.*

Commission answer: Data on bioaccessibility or bioavailability are only useful if a direct relation is present or can be established with the mechanism of toxicity under consideration. Thus for the read-across between nickel compounds the mechanism for e.g. acute toxicity and carcinogenicity is not known and data on bioaccessibility or bioavailibility are not helpful. For sensitisation (local bioaccessibility) or reproductive toxicity (systemic bioavailibility) data on these parameters may be useful, in order to evaluate the potential for this effect.
It is not correct that water solubility alone is the basis for the read-across approach. The category approach used starts by grouping nickel compounds in a number of subcategories on the basis of their water solubility as the toxic effect of nickel is caused by the dissolved Ni^{2+}-ion. The sub-categories are a) very soluble and soluble compounds, b) sparingly soluble compounds (e.g. nickel hydroxycarbonate), c) insoluble compounds with solubility comparable to the nickel sulfides, d) insoluble compounds with solubility comparable to the nickel oxides and e) metal-metal compounds. The nickel substances were divided between these groups based on either specific water solubility data or by predicting the water solubility based on information on water solubility of the Ni–ligands formed. The predictions for water solubility were based on information obtained for different types of Ni-ligands formed from the different Ni compounds. These sub-categories, with the exception of (b), the sparingly soluble compounds have traditionally been used as a basis for grouping nickel compounds[13]. In establishing these sub-categories, compounds that would not be expected to behave similarly to the nickel compounds used for comparison were excluded either as part of the original proposal or in the subsequent discussion. The approach recognises that water solubility is a predictor for systemic bioavailability of nickel but not necessarily for bioavailability in lung tissue where specific up-take mechanism may operate. For each toxicological end-point a specific decision was made whether read-across could be justified.

For the group of water-soluble compounds, the assumption has been made that there will be sufficient oral absorption of these compounds to justify classification for systemic effects such as germ cell mutagenicity and reproductive toxicity. There is no evidence to suggest that this assumption is not justified[14]. For some compounds in the sparingly water-soluble subcategory the bioavailability is increased due to the acidic conditions of the stomach e.g. nickel hydroxycarbonate, nickel hydroxide. For the remaining substances in this subcategory

[13] These sub-categories (with the exception of the sparingly soluble group) were used by NiPERA in their 1996 proposal for EU OELs to the Directorate General Employment of the European Commission.
[14] It is possible that this is a conservative evaluation for certain soluble compounds, as the uptake may be lower for some than for others. This is however very similar to the approach used in the Voluntary risk assessment for copper compounds and SCHER has stated their agreement with this approach in their opinion on the copper Voluntary risk assessment.

the potential for systemic effects are not considered. They are not considered for the other subcategories of lower water solubility[15].
The evidence for skin sensitisation suggests that even compounds with extremely low water solubility such as nickel oxide release enough nickel to justify classification as a skin sensitiser. The use of additional bioaccessibility data for this effect has been used to demonstrate that certain crystal structures such as spinel or rutiles do not release enough nickel to justify classification[16].
The mechanisms of lung cancer and chronic lung irritation are not fully understood. Data on bioaccessibility or bioavailability are only useful if a direct relation is present or can be established with the mechanism of toxicity under consideration. As both effects are seen across the whole range of water-solubility shown, the classification for these effects is not based directly on considerations of water-solubility but on the scientific consensus on the appropriateness of read-across for carcinogenicity[17].
Read-across for the systemic effects of acute toxicity and for local effects of skin irritation have not been included in the proposal. The mechanism for acute toxicity is not known, and a quantitative measure is required for a correct classification[18].Both endpoints are covered by Note H, and classification for these effects remains the responsibility of the supplier[19]

- *The classification of nickel compounds is based on very few scientific information as for most of the nickel substances there is not any scientific information on the toxicological effects and there is no scientific information that demonstrates that nickel substances with similar water solubility would cause similar toxicological effects.*

Commission answer: The division of nickel compounds into different solubility subcategories is intended to ensure that comparisons are made with as comparable nickel compounds as possible. In addition, water solubility is a well accepted surrogate for bioavailability. Please find hereafter an extract of a document from Eurometaux, Eurofer and ICMM (International Council on Mining and Metals**)** (http://www.ebrc.de/ebrc/downloads/HERAG.pdf): "In risk assessment for a wide range of metal compounds, extrapolation between different metal compounds is necessary and the fact sheet gives the following recommendations: • For a differentiation between soluble vs. poorly soluble or insoluble forms, water solubility is often used as a surrogate for bioavailability. For example in the assessment of nickel and zinc, it has been experimentally verified (in vivo) that large variations exist between soluble salts of a metal, and the metal itself, or the oxides or other very poorly soluble substances. This principle has also been established for cobalt, based on in vitro data."

[15] The classification proposal in the lead voluntary risk assessment (which has not yet been discussed by the TC C&L) includes a classification for all inorganic lead compounds even in cases where there is no data on bioavailability.

[16] This conclusion is consistent with the formation of spinel and rutile compounds on the surface of stainless steel alloys where no skin sensitisation is seen after direct and prolonged contact.

[17] As reflected in the opinion of the Specialised Experts in 1990 and 2004, IARC in 1990, CSTEE in their oipinion on Ambient Air Quality and SCHER in their opinion on the ESR Risk Assessment reports.

[18] It should be noted that the change from Directive 67/548/EEC criteria to GHS criteria for this endpoint results in a change of cut-off between classification bands, and will lead to different classification under the two systems.

[19] It should be noted that this is entirely consistent with the approach laid out both the Title in REACH on classification and in the draft Classification, Labelling and Packaging Regulation that Harmonised classifications should address primarily effects such as cancer, mutagenicity, reproductive toxicity and respiratory sensitisation.

The approach used is entirely consistent with the approach used in other group classifications in Annex I, where expert judgement has been regarded as a sufficient basis for classification of similar chemical substances (organic as well as inorganic). The main difference in these proposals is the explicit use of sub-categories to reflect the differences in bioavailability across the range of water solubility for the compounds.

- *The classification of nickel compounds is based on a category approach that does not follow the OECD guidance on grouping (e.g., confirmatory testing step is missing).*

Commission answer: The grouping approach followed the guidance given by the OECD in this area. As the EU legislation does not require testing for the purposes of classification, the step of the OECD guidance where the grouping approach may be confirmed by testing could not be applied. However, where such confirmatory testing would have been necessary to establish the scientific validity of the group, it was decided not to classify for specific effects (*e.g.*, acute toxicity) or specific substances (*e.g.*, Nickel compounds with certain crystal structures such as spinel or rutiles).

- *The classification of nickel compounds should be done in the framework of REACH and the up coming CLP Regulation in order to consider the information that should be submitted by Industry in the framework of their testing program on bioaccessibility.*

Commission answer: The new data and the data generation programme proposed by industry have been carefully studied by the Commission and the EU Member State experts. The new information does not influence the conclusions on the classification and the testing programme, which goes further than the requirements set out in REACH, will take several years to finish and is doubtful to influence the assessment. As the approach is a refinement of approaches applied over the past many years, which has also been supported by different scientific committees, the Commission is of the view that the assessment is based on sound science. As it is not likely that the new data will change the conclusions of the assessment in the shorter term, it is not likely that the proposed strategy by industry will alter the conclusion of our assessment. Hence not adopting the 31st ATP with the nickel compounds will not only be contrary to the Commission's obligations to act swiftly when identifying carcinogens, but also deprive users of such substances from the information which would enable them to handle the substances safely. However, when the scientific data gathered by Industry will become available, they will be assessed to see if the classification of Nickel compounds has to be modified.

- *Nickel arsenide (CAS Number 12255-80-0) should not be classified for acute toxicity.*

Commission answer: Nickel arsenide (CAS Number 12255-80-0) is not included in the proposal. However, for acute toxicity, in the 31st ATP the Note H applies. This means that Industry should decide on the classification for this effect on the basis of available data.

- *Perchloric acid, nickel(2+) salt (CAS Number 13520-61-1) should be classified as corrosive.*

Commission answer: Perchloric acid, nickel(2+) salt (CAS Number 13520-61-1) is not included in the proposal. However, perchloric acid, nickel(II) salt (CAS RN 13637-71-3) is proposed to be classified as corrosive in the 31st ATP.

- Nickel nitrate (CAS Number 13138-45-9) should be classified as irritant to the eyes.

Commission answer: Nickel nitrate (CAS Number 13138-45-9) is not included in the proposal, but it is included in the 30th ATP as irritant to the eyes.

*** Trade/economic concerns**

The classification of nickel compounds
- would negatively affect their industries and their exports of nickel and other by products,
- would restrict a signification proportion of their trade,
- would negatively impact their economic growth and development,
- would constitute an unnecessary barrier to trade and is therefore not in line with article 2.2 of the TBT agreement,
- would potentially contribute to the stigmatisation of nickel and nickel containing material,
- could reduce research and investment in important nickel-based technologies and material,
- is inconsistent with the objective of the TBT Agreement,
- would reduce the supply of nickel substances to downstream users and damage the competitiveness of manufactures in critical sectors (e.g., iron steel industry) that rely on nickel substances.

Commission answer:

Some nickel compounds have been classified by the European Union since 1993 and even listed under Directive 96/82/EEC on the control of major-accident hazards involving dangerous substances (the Seveso II Directive) and this has not resulted in any complaint from the nickel industry about a reduction in the trade of these compounds. In the same way, IARC (International Agency on Research on Cancer) concluded in 1990 on the basis of overall evaluation that Nickel compounds are carcinogenic to humans (see http://www.inchem.org/documents/iarc/vol49/nickel.html). The IARC Working Group made the overall evaluation on nickel compounds as a group on the basis of the combined results of epidemiological studies, carcinogenicity studies in experimental animals, and several types of other relevant data supported by the underlying concept that nickel compounds can generate nickel ions at critical sites in their target cells.The TBT Agreement lists in Article 2.2 the protection of human health and safety as legitimate objectives that Members can pursue when developing technical regulations. The 31st ATP has these objectives as its basis. As set out above, the proposed measures do not create unnecessary obstacles to international trade and are not more trade-restrictive than necessary to fulfil their legitimate objective. Health and safety will be assured by the information that will be provided on the label. In fact, with the adoption of the UN Globally Harmonised System of Classification and Labelling (GHS) there is a global agreement that substances having proven hazardous properties should be labelled accordingly. The EU harmonised classification and labelling implements this approach. As there is a world wide agreement that such labelling information is necessary to safeguard users of the substances against unwanted risks, we do not see major trade problems as a result. In this context it is important to stress that the labelling requirement only concerns the substance and mixtures containing the substances and does not affect articles.

*** Downstream consequence**

- The classification of nickel compounds would trigger a series of downstream regulatory requirement which would impose additional restriction, prohibitions or substitutions of nickel substances under REACH and other EU legal instruments.

Commission answer: Industry and some third countries have argued that the classification would have serious consequences under REACH, in particular, that all such compounds would have to be authorised. Under Regulation (EC) No 1907/2006 on Registration, Evaluation, Authorisation and Restrictions of Chemicals (REACH), substances classified as CMR category 1 or 2 will indeed be potential candidates for authorisation. However, it is important to note that the authorisation requirement applies neither directly nor automatically. The process of identifying substances to be subject to authorisation consists of two steps (the establishment of the candidate status of the substance and then, the prioritisation of the substance for the actual authorisation procedure) which are subject to scientific evaluations following transparent scientific procedures. If a substance meets the criteria for classification as carcinogenic, mutagenic or toxic to reproduction category 1 or 2 (CMRs) in accordance with Directive 67/548/EEC, the step to identify the intrinsic properties may be limited, if appropriate, to a reference to an entry in Annex I of Directive 67/548/EEC. In addition, REACH provides for the possibility of exemptions to the obligation to obtain authorisations for certain uses or categories of uses. Authorisation will be given either on the basis of adequate control of the risks, or on the basis of a socio-economic analysis proving that the benefits from the substance's use outweigh the risks it poses to human health or the environment and that there are no suitable alternative substances or technologies.

Several countries have pointed that the classification would mean that the use of nickel in certain products (metal plating cutlery etc) would be restricted. As noted before, this is not the case since the proposed classification does not affect directly the marketing of and trade in end-products containing such nickel compounds, but only their transport marketing and handling as separate substances or mixtures.

A quasi-automatic restriction (i.e., fast-track procedure) for the marketing and use of substances classified as CMRs category 1 or 2, as currently foreseen under Directive 76/769/EEC and in Article 68, paragraph 2, of REACH, is limited to substances or preparations sold to the general public above the concentration limits specified in Annex I to Directive 67/548/EEC (as amended and adopted to technical progress).

In cases where restrictions on the supply to the general public are likely to have a significant impact on industry, the European Commission always carries out an impact assessment to ensure that the restrictions are proportionate to the reduction of the risk. Such an impact assessment would also take into account the socio-economic impact of the restriction, including the availability of alternatives.

In this context, it is worth noting that Nickel is a well known allergen. It is therefore unlikely, that there are today still many consumer products on the market which contain Nickel compounds.

Industrial or professional use(s) of those substances or preparations will not be restricted in this quasi-automatic way. They will be subject to the provisions of Title VIII of REACH. However, it has to be said, that certain downstream legislation like for example the one on workers protection, foresees more severe measures when substances classified as CMRs,

category 1 or 2 are used in the production process.If a restriction of its use in end-products through Directive 76/769/EEC or through REACH is envisaged, it would also be subject to a separate notification under the TBT Agreement.

Directive 76/768/EEC on the approximation of the laws of the Member States relating to cosmetic products (the Cosmetics Directive) already covered Nickel compounds due the allergenic potential of nickel. Therefore, the ban of nickel compounds in cosmetic products due to their classification as carcinogens category 1 should not have a big impact on Industry and WTO countries.

- *The classification of nickel compounds would have consequence on the requirement for the transportation of nickel compounds.*

Commission answer: International transport rules do not forbid transport of substances having CMR properties. Transport legislation does not require labelling for chronic hazards, but only for acute ones.

- *The classification of nickel compounds would have consequence on the storage of nickel compounds and would require an authorisation under the Seveso Directive.*

Commission answer: It is true that Nickel compounds due to the proposed classification in the 31st ATP, in particular the classification as R50: 'Very toxic to aquatic organisms' (including R50/53), will fall under the Seveso II Directive. The thresholds for this category are 100/200t. The Seveso II Directive applies to establishments in all EU Member States according to the quantity of dangerous substances present: only some requirements apply to plants with 100 to 200 tonnes (lower-tier establishments), in particular notification, major accident prevention policy, inspections; all requirements apply to those plants which contain more than 200 tonnes (upper-tier establishments), in particular a safety report including a description of the possible major-accident scenarios. It should be noted that some Nickel compounds appear already in the Seveso II Directive as named substances "Nickel compounds in inhalable powder form (nickel monoxide, nickel dioxide, nickel sulphide, trinickel disulphide, dinickel trioxide), with a threshold of 1 tonne.

7) CONTENT OF THE DIRECTIVE

7.1) General Issues

Article 1

This article amends Annex I to Directive 67/548/EEC.

Article 2

This article imposes the deadline to transpose the amendments to Annexes I into national legislation.

Article 3

This article states that this directive will enter into force 20 days after its publication in the Official Journal of the European Communities.

Article 4

This article makes clear that this directive is addressed exclusively to the Member States.

7.2) ANNEXES

Annex 1A

This annex modifies Annex I to Directive 67/548/EEC.

Annex 1B

This annex modifies Annex I to Directive 67/548/EEC.

Annex 1C

This annex modifies Annex I to Directive 67/548/EEC.