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Paris, 12th May 2010

Dear Sirs,

Your draft publication **SKIN NOTATION(SK) PROFILE METALLIC CHROMIUM AND OTHER SUBSTANCES CONTAINING HEXAVALENT CHROMIUM [Cr(VI)]** has come to our attention and our comments on it are attached along with other documents relevant to the topic.

The International Chromium Development Association(ICDA) represents the global chromium industry with more than 100 members covering the various industrial sectors. ICDA operates a number of standing committees including one dealing with health, safety and environment which consists of representatives who are suitably qualified in the relevant disciplines.

Further information regarding the Association can be found on www.icdachromium.com .

In summary, it is our opinion that the various generic health effects notations shown for chromium are inappropriate since the various adverse health effects listed are specifically attributable to chromium in its hexavalent state as encountered in chromates, dichromates and chromic acid(CrO_3) and not to chromium in its metallic state or to substances containing chromium in its trivalent state.

We look forward to hearing your response but if you have any questions or wish more information please do not hesitate to contact the undersigned.

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RESPONSE TO NIOSH DOCUMENT SKIN NOTATION(SK) PROFILE METALLIC CHROMIUM AND OTHER SUBSTANCES CONTAINING HEXAVALENT CHROMIUM [Cr(VI)]

BACKGROUND

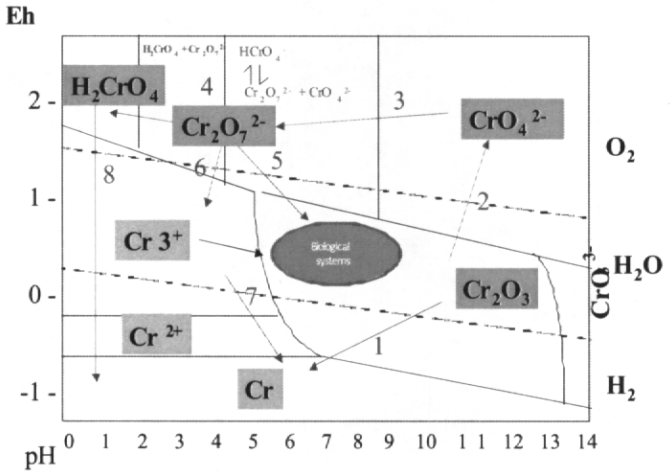
Any notation regarding adverse health effects of any chemical element or substance must be based on the realistic interpretation of sound science recognising that where an element can exist in different valency states, specific states may exhibit specific behaviours and therefore generic notations referring only to the element may well be inappropriate and misleading.

The element chromium is a particularly good example of species-specific nature of adverse health effects.

With the exception of the very rare mineral crocoite, lead chromate, containing chromium in the hexavalent state, chromium occurs naturally in the trivalent(Cr^{3+}) state principally in the mineral chromite $[Fe^{II},Mg](Al,Cr,Fe^{III})_2O_4$. Chromite is the raw material used in the commercial manufacture of industrial chromium chemicals and the alloy ferrochromium (FeCr).

Hexavalent chromium resulting from human activity is mainly encountered in chromates containing the CrO_4^{2-} ion, dichromates containing the $Cr_2O_7^{2-}$ ion, chromium trioxide(CrO_3) .The "bare" hexavalent chromium cation does not exist but rather as an oxyanion within the pH boundary of biological systems-see species stability domain diagram below.

POURBAIX DIAGRAM FOR CHROMIUM



Taken from Barnhart, Reg. Toxicol. Pharmacol., 1997,**26**,53

Chromium in the metallic state(Cr^0) is produced either by electrolysis of solutions containing chromium trioxide or trivalent chromium, by the aluminothermic, carbothermic or silicothermic reduction of chromium(III) oxide or as ferrochromium by carbothermic reduction of chromite in electric arc furnaces.

Metallic chromium is only stable in the hydrogen domain and is not bioaccessible. The surface in contact with air undergoes spontaneous oxidation to Cr_2O_3 which effectively passivates the surface from which minute quantities of Cr(III) are released on exposure to biological systems. This characteristic is also responsible for the corrosion resistance of stainless steels.

Examples of reviews that demonstrate the species-specific nature of chromium toxicity include ATSDR(2008), EU(2005) and ICDA(2006).

Occupational exposure limits for chromium(0) and chromium(III) are typically 10-100 times higher than those for chromium(VI).

Therefore it is reasonable to expect that any notation that indicates the realistic potential for an adverse effect due to chromium exposure includes reference to the specific species involved otherwise that notation is likely to be misleading.

Chromium without any indication of valency state is assumed to mean chromium in its metallic or zero-valent state.

COMMENTS ON THE NIOSH DOCUMENT

The title infers that metallic chromium contains hexavalent chromium. It does not.

This inference appears at various points in the document.

Throughout the document there are many references to adverse health effects of chromium without any designation of species. This is misleading.

1.1 General Substance Information

Chemical-see above comment.

CAS No: 7440-47-3 refers to chromium metal; 18540-29-9 refers to hexavalent chromium, not any specific substance containing hexavalent chromium-see EU(2005)

Molecular formula: specific to the substance in question.

Structural formula: specific to the substance in question.

Synonyms: Chrome and chromium are synonymous; Hexavalent Chromium, Chromium(VI) ion and chromium(VI) are synonymous but not with Chrome or chromium; Chromium ion is meaningless without designation of the valency state of chromium; Chromic ion usually infers Chromium(III) and is not synonymous with any of the others.

1.2 Overview of SK Assignment for Cr

All of the effects identified in this section including Table 1 are attributable to exposure to substances containing hexavalent chromium and not chromium unspeciated. It is known that

exposure to soluble chromium(III) will elicit a skin reaction in subjects previously sensitised to hexavalent chromium.

All of the examples cited showing systemic toxicity including the LD_{50} values refer to substances containing hexavalent chromium.

The studies of Filon et al(2008,2009) refer to exposure of skin to chromium metal powder in vitro. Chromium is released in the trivalent state from the metal-see above. The data cited should be compared with the following: the upper limit of the safe range of population mean intakes could be above 250µgCr/day(WHO,1996); Estimated Safe and Adequate Daily Dietary Intake (ESADDI) for chromium for children of 7 years to adult is 50-200µg/day(NRC,1989); Reference Daily Intake for chromium 120µg/day(FDA,1995); intravenous injection of chromium(III) hexa-urea chloride into male Sprague-Dawley rats resulted in an LD_{50} of 10mgCr/kg(Mertz et al, 1965); the same study showed an LD_0 of 5mgCr/kg.

The finding that significant amounts of chromium is fixed in the skin(Filon,2008,2009) is not surprising since secure binding of trivalent chromium to collagen is the basis for the dominance of the use of salts containing chromium(III) in leather tanning.

A generic Cr notation for systemic toxicity does not seem appropriate.

Table 2, Summary of the carcinogenic designations for Cr by numerous governmental and nongovernmental organisations is misleading again because of the non-speciated reference to chromium. All of the published animal and epidemiology evidence points to the carcinogenicity of substances containing hexavalent chromium. IARC concludes that: Chromium(VI) is carcinogenic to humans-group 1; there is inadequate evidence for the carcinogenicity of Chromium(III) compounds or Metallic chromium in animals or humans. EU(2005) reviews the health effects of a group of 5 substances containing hexavalent chromium and reaches conclusions regarding hazard classification for a range of endpoints.

ICDA(2006) reviews health effects of metallic chromium and trivalent chromium.

3.0 Direct Effects on the Skin (SK:DR)

All of the studies cited which caused adverse effects including ulceration describe exposure to substances containing hexavalent chromium. Direct effects of chromium(VI) and consequences regarding hazard classification are included in EU(2005) and for metallic chromium and trivalent chromium in ICDA(2006).

In EU(2005) a distinction is made between the direct skin contact effects of chromates and dichromates and those of chromic acid.

On the basis of the available evidence the SK:DR (COR) notation should be assigned to Cr(VI).

4.0 Immune-mediated Responses

The ability of substances containing hexavalent chromium to cause both skin and respiratory sensitisation is not in doubt and such substances are classified accordingly(EU,2005).

According to Lidén et al(2001) chromium metal does not act as a hapten. The minute amounts of chromium(III) that are released from the surface of the metal and chromium containing alloys such as stainless steels do not induce chromium sensitisation and do not elicit allergic reactions in subjects previously sensitised to chromium.

Again the generic notation that Cr is assigned SK:SEN is not appropriate.

5 Summary

Inferences that chromium, not speciated, is capable of causing the adverse effects listed are misleading and are not supported by the available evidence. The composite skin notation SK: SYS-DIR(COR)-SEN is perhaps appropriate for substances containing hexavalent chromium but not for chromium without any indication of speciation.

Table 3 is correct insofar that data available for chromium in its metallic state do not justify any skin notation.

What the table overlooks is the fact that the hexavalent chromium substances which have undergone risk assessment in the EU(EU,2005) have been correctly classified for effects resulting from skin contact.

References

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