Science-based review of the Proposal for Harmonised Classification and Labelling of Divanadium pentaoxide (CLH Report, Version 02, August 2019) by Dr. David. J White

DISCUSSION:

As a qualified and experienced vanadium chemist, I have reviewed the document **CLH Report – Proposal for Harmonised Classification and Labelling – Divanadium Pentaoxide (August 2019)** and believe it needs major revisions to adhere to what is commonly known and accepted about vanadium chemistry. (Crans and Tracey, 1998; Crans et al 2004, Nriagu, 1998a and Nriagu 1998b)

The proposal for divanadium pentaoxide (V_2O_5) classification as written is not valid as it does not limit itself to data on V_2O_5 but rather includes data from other vanadium compounds. While 'read across' from one compound to another similar compound is widely used to make informed interpolations to fill knowledge gaps, it is wholly unacceptable to use data on other compounds to set regulatory classifications for a specifically named chemical. Such an approach risks applying regulatory determinations to very different compounds leading to either under or over regulation. Further, the proposal does not fully take account of the fact that V_2O_5 does not exist in an aqueous environment and the resulting compounds from the reaction of V_2O_5 with water are highly dependent on the test conditions (Crans and Tracey, 1998).

1) **VANADIUM CHEMISTRY**. The inorganic chemistry of vanadium is varied and complex and this must be considered in evaluating the relevance and reliability of studies.
   a) In particular, the aqueous chemistry of vanadium between pH 0 and 14, with concentrations 10^1 to 10^{-10} mol/dm^3 V and at different redox potentials, spans at least 23 species in 4 oxidation states with 9 different molecular charges (even before consideration other interacting chemicals and ligands that might be encountered in biological or environmental systems). None of these species are V_2O_5 which instead rapidly reacts with water to form yellow acidic solutions.
   b) In contrast to direct exposure to $V_2O_{5(s)}$, utilizing studies involving solutions made by adding V_2O_5 to a solution (for example water, buffered water or actual or simulated biological fluids) cannot be assumed to be V_2O_5. Divanadium pentaoxide reacts with water according to the equation:

$$V_2O_{5(s)} + 3\ H_2O_{(l)} = 2\ H_3VO_{4(aq)}$$

   And the resulting solutions can be highly acidic depending on the concentrations and conditions used. This low pH can have biological effects irrespective of the presence of vanadium.
   c) At concentrations above 1mM condensation reactions begins to occur to form aqueous species such as $[V_2O_7]^{4-}{}_{(aq)}$ and $[V_{10}O_{28}]^{6-}{}_{(aq)}$. Therefore, studies on 'solutions' of V_2O_5 need to be carefully considered as to their relevance in assessing the classification and labeling of divanadium pentaoxide.

2. **STUDIES AND DATA ON COMPOUNDS OTHER THAN DIVANADIUM PENTAOXIDE.** Any valid review must be careful to only include studies relevant to V_2O_5 or provide a clear basis (such as data that the other compound occurs in the metabolic pathway) for inclusion. For example:
   a) Other vanadium chemicals have considerably different chemical and physical properties. The dossier itself acknowledges on page 15, Table 9 that the four vanadium compounds mentioned there have solubilities ranging from 0.15 mg/L to "very soluble" and it cannot be assumed that such disparate chemicals would have similar toxicological effects.
   b) On page 11 of the dossier it is state that "REACH registration dossiers for divanadium pentaoxide and vanadates, available from ECHA's disseminated database have been analysed for study references, which have then been considered as data sources for the CLH report". This use of data from non V_2O_5 studies, e.g. Bogden et al (1982) see page 17 of the dossier, is improper and potentially invalidates the entire dossier.
   c) Of even more concern is the consideration of vanadium compounds in other oxidation states, for example on page 48, Edel and Sabbioni (1989), which considers pentavalent and tetravalent forms, must be handled with extreme care.
   d) On Page 18 the dossier opines "In the lung, divanadium pentoxide should therefore be discriminated from other vanadium compounds with higher solubilities". From both a technical and regulatory perspective this discrimination should be respected throughout the assessment, eliminating data on other vanadium compounds, e.g. table 25, or data where speciation is undetermined, e.g. Table 24.
   e) Several occupational exposure studies are considered in the proposal. Extreme caution should be exercised in including these in the assessment. For example, the Ehrlich study (Ehrlich, 2008), (page 44, Table 17) relates to a plant that manufactured multiple metal containing products. Note there is no data to identify divanadium pentaoxide, only measurement of blood vanadium with no speciation or data on evidence that could correlate it to V_2O_5 exposure. Workers were exposed to metal containing raw materials, intermediate products and finished materials, but also to other chemicals used in the production process and to other chemical elements and compounds contained in the raw materials. Correlating observed effects only to divanadium pentaoxide exposure without a detailed and careful analysis of other potential confounders cannot be justified. Such studies cannot be included in the assessment of vanadium pentoxide without evidence of exposure. Note also that vanadium levels in the blood did not correlate with the lesions which the authors noted (Ehrlich, 2008).

CONCLUSION:

In view of the specific vanadium chemistry described above, the dossier should be, at the very least, be significantly revised with only studies and information pertinent to V_2O_5 included. Further, a more careful assessment of the toxicological studies referenced in the report should be made to ensure that those purporting to be on V_2O_5really are on V_2O_5. These reviews should be carried out by a qualified inorganic chemist with relevant experience of vanadium.

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The views expressed in this Review are solely those of the author and do not necessarily express the views of the Vanadium Producers and Recyclers Association or any other organisation or person.

SHORT BIOGRAPHY:

Dr. David White was born in the United Kingdom and attended Oxford University where he obtained Bachelors, Masters and Doctoral degrees in Chemistry, specializing in the inorganic chemistry of metals. While at Oxford he held a lectureship in Inorganic Chemistry at Exeter College. He then carried out postdoctoral research at the University of California, Berkeley and Edinburgh University. During this time, he was a co-author of over 20 peer reviewed publications and presentations. He then started a 20-year industrial career focused on the mining and processing of minerals and metals, reaching senior executive levels. This included 13 years in the Vanadium industry, with a focus on environmental stewardship and safety and was Chairman of the International Vanadium Industry Health, Safety and Environment Committee.

Dr. White is currently proprietor of David White Chemical and Metallurgical Consulting based in Raleigh, NC. He has been elected a Member of the Royal Society of Chemistry (UK) and holds Chartered Chemist status. He holds both United Kingdom and United States citizenship.