National Institute of Environmental Health Sciences (NIEHS)
Comments on the Interagency Science Discussion (Step 6)
Draft IRIS Toxicological Review of Hexavalent Chromium [Cr(VI)]
June 2024

Date: 06/28/2024

Page 3-211, Section 3.2.5 Hematological effects

- First paragraph, Line 11. Regarding sentence "Hematology along with clinical pathology measures (e.g., blood proteins, 11 enzymes, chemicals and waste products) and other general health status indicators are useful…". Suggest adding the word "other" before clinical pathology measures. I.e., "Hematology along with ***other*** clinical pathology measures (e.g., blood proteins, enzymes, chemicals and waste products) and other general health status indicators are useful…"

  Clinical pathology measures include hematology (hematology is a subgroup of clinical pathology as stated in the first sentence of the paragraph). Alternatively, the sentence could be changed to read "Hematology along with clinical ***chemistry measurements*** (e.g., blood proteins, enzymes, chemicals and waste products) and other general health status indicators are useful…"

Page 3-211, Table 3-29

- As indicated in a previous NIEHS comment, modern hematology machines (past 50+ years) directly measure MCV either by impedance or optically. Thus, even though MCV can be calculated using the Wintrobe equation listed in the table, that is no longer how MCV is "measured" and the reason for including the equation is not clear and could insinuate that that MCV was calculated vs. being directly measured. With modern hematology analyzers, hematocrit, MCHC and MCH are calculated indices using the directly measured indices of hemoglobin, RBC count and MCV.
- Excess iron is not known to cause macrocytic RBCs. Suggest removing this comment. Macrocytosis is seen with regenerative anemias (reticulocytes are larger in size) and with dyserythropoietic disorders such as folate/cobalamin deficiencies, erythroleukemia and myelodysplastic syndromes.

Page 3-212, Table 3-29

- Suggest removing mention of high MCHC: hyperchromic. In theory and presumed to be true, it is not physiologically possible to produce hyperchromatic erythrocytes because hemoglobin synthesis stops in an erythrocyte precursor when an optimal hemoglobin concentration is reached within the cytoplasm. The vast majority (or all) of increased MCHCs is spurious and CHCM is more reliable when pre-analytical or analytic conditions, or clinical disease is such as to cause an increase MCHC. Examples of what cause falsely increased MCHC include: in vitro hemolysis, spectral interferences in the blood hemoglobin assay, and red cell shrinkage due to in vivo hyponatremia.

Note: The scientific review and comments are provided by National Institute of Environmental Health Sciences (NIEHS) Division of Translational Toxicology scientists and are not intended to represent formal agency position or opinion.