AGENDA

Adobe Connect Webinar
September 19 and 25, 2013
9:30 am – 12:30 pm EDT
visit the workshop website

Discussion Focus

Day 1: Reduction, absorption, and transit of ingested hexavalent chromium in the human GI tract

The first workshop session will focus on questions regarding the toxicokinetic properties of ingested hexavalent chromium that will inform estimates of the amount absorbed in unreduced form in different portions of the GI tract as a function of species and dose.

Day 2: Factors affecting susceptible human populations and lifestages

The second workshop session will focus on questions addressing what is currently known about how toxicokinetic processes may vary among human populations and/or lifestages and potentially impact susceptibility to hexavalent chromium-induced toxicity.

Panel

Co-Chairs:
- Gary Ginsberg – *Connecticut Department of Public Health*
- Elaina Kenyon – *EPA ORD NHEERL*

Panelists:
- Kim Barrett – *University of California, San Diego*
- Max Costa – *New York University*
- John Crison – *Bristol-Myers Squibb*
- Silvio De Flora – *University of Genoa*
- Sean Hays – *Summit Toxicology*

Workshop Overview

Chromium exists in multiple oxidation states, but two forms are most prevalent biologically – hexavalent chromium (also known as chromium 6) and trivalent chromium (also known as chromium 3). When ingested, hexavalent chromium can be reduced to trivalent chromium by a number of reducing agents within the gastrointestinal (GI) tract, but the reverse of this process, oxidation of trivalent to hexavalent chromium, will not occur in the human body. Hexavalent chromium is a known human carcinogen when inhaled and has been shown to cause tumors in mice and rats when ingested in drinking water, but there is little evidence indicating that ingesting trivalent chromium, a dietary supplement, poses any toxic or carcinogenic risk to humans. This is because extracellular trivalent chromium is poorly absorbed by cells, whereas extracellular hexavalent chromium is readily taken up by cells. Hexavalent chromium is toxic only after it is absorbed by the cells and then reduced (inside the cell) to trivalent chromium. Consequently, ingested hexavalent chromium that is reduced to trivalent chromium outside of the cells lining the GI tract – before being absorbed by these cells – is effectively detoxified. Hexavalent chromium that is not reduced to trivalent chromium outside of the cells lining the GI tract is readily absorbed by these cells. Therefore, it is important to understand these two simultaneous and competing processes – absorption of hexavalent chromium by cells lining the GI tract and reduction of hexavalent chromium to trivalent chromium outside of the cell – since they are an important part of evaluating the cancer causing potential of ingested hexavalent chromium in humans.

To inform EPA's ongoing IRIS assessment of hexavalent chromium, EPA has invited experts representing scientific areas related to the reduction and absorption of ingested hexavalent chromium, including metals chemistry, toxicokinetics, and GI physiology and pathology to serve on a panel. Panelists will prepare and present discussion topics that will aim to highlight what is known and what remains unknown about the topic in relation to human cancer risk from ingested hexavalent chromium. This format will encourage scientific discussion about how current knowledge can be applied to the IRIS assessment of hexavalent chromium and how knowledge gaps might be filled to reduce uncertainty in the analysis.

The same panel will convene for both workshop sessions and will not seek to reach a consensus on any discussion topic.

Thursday September 19

Welcome and Introductions	
9:30 am EDT	EPA Introduction and Overview
9:40 am EDT	Introduction of Panelists and Co-Chairs
Discussion: Toxicokinetics and Uncertainty	
9:50 am EDT	Discussion Topic 1: Regional absorption Lead discussant: Dr. Max Costa
10:20 am EDT	Discussion Topic 2: Reduction mechanisms Lead discussant: Dr. Sean Hays
10:50 am EDT	Break
11:00 am EDT	Discussion Topic 3: Gastrointestinal pharmacokinetics Lead discussant: Dr. John Crison
11:30 am EDT	Discussion Topic 4: Gastrointestinal toxicity markers General discussion (time permitting)
Public Input	
12:00 pm EDT	Public Input/Questions
12:30 pm EDT	Meeting Adjourns

Wednesday September 25

Welcome and Introductions	
9:30 am EDT	Introduction of Panelists and Co-Chairs
9:35 am EDT	Review Day 1 Discussion Topics
Discussion: Susceptibility	
10:00 am EDT	Discussion Topic 5: Disease states and medical factors Lead discussant: Dr. Kim Barrett
10:40 am EDT	Discussion Topic 6: Dietary and nutritional factors General discussion
11:20 am EDT	Break
11:30 am EDT	Discussion Topic 7: Lifestages General discussion
Public Input	
12:10 pm EDT	Public Input/Questions
12:30 pm EDT	Meeting Adjourns