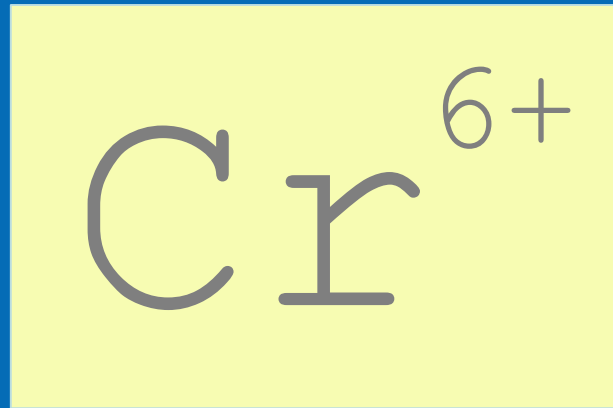


# Preliminary Materials for the IRIS Assessment of Hexavalent Chromium (Part II)

*Catherine Gibbons, Ph.D. and Alan Sasso, Ph.D.,  
Assessment Managers*



# IRIS assessment of Cr(VI): Timeline

---

## **1998** Cr(VI) Toxicological Review posted to the IRIS database

- *Known human carcinogen* by inhalation; *not classifiable* by ingestion
- Includes RfD, RfC, and IUR; no OSF

## **2008** NTP 2-yr bioassay of Cr(VI) in drinking water

- *Clear evidence* of carcinogenic activity
  - Oral cavity tumors in male and female rats
  - Small intestinal tumors in male and female mice
- Prompts EPA program offices and regions to nominate Cr(VI) for reassessment by IRIS
- Focus on oral exposure

# IRIS assessment of Cr(VI): Timeline

---

**2010** External Peer Review draft of the IRIS assessment (oral exposure only) is posted

**2011** External Peer Review meeting on the 2010 draft assessment

- ACC presents research plans during public comment period
- Several panelists recommend waiting for ACC-funded studies to be completed

# IRIS assessment of Cr(VI): Timeline

---

**2013** IRIS conducts a workshop on issues regarding gastrointestinal reduction, absorption, and transit of ingested Cr(VI) in rodents and humans, including susceptible subpopulations

**2014** IRIS releases two preliminary packages for Cr(VI)  
–Scope of assessment expanded to include both oral and inhalation exposures

# Bimonthly Meetings for Cr(VI)

## Preliminary Package for Cr(VI), Part 1 (June 2014)

- Science questions related to:
  - Problem formulation
  - Evidence from experimental animal studies

## Preliminary Package for Cr(VI), Part 2 (today)

- Science questions related to:
  - Evidence from human studies
  - Toxicokinetic studies
  - Mechanistic studies

# Cr(VI) Science Questions for the October IRIS Bimonthly Meeting

- Methodological considerations for evaluating epidemiology studies
- Inhalation cancer dose-response modeling
- Toxicokinetic considerations for dose-response
- Mechanistic studies database
- Chromium-DNA adducts
- In vitro/in vivo mutagenicity/genotoxicity studies
- Definitions of mutagenicity and genotoxicity

# **Science Question 1: Methodological considerations for evaluating epidemiology studies**

# Overview of Human Literature

- Exposure setting: occupational studies

- Chromium/chromate production workers
- Chrome plating workers
- Stainless steel manufacturing
- Welding
- Electroplating
- Plastics
- Boilermakers
- Aerospace
- Leather tanneries

- Exposure measure:

- Job description/ duration of employment
- Job exposure matrix
- Area and personal air sampling
- Biological samples



# Primary Human Health Outcomes for Hazard ID

## Inhalation

### Hepatic effects (Section 2.3)

- liver cirrhosis mortality
- ALT, ALP, AST levels

### Hematological effects (Section 2.4)

- RBC, Hb, platelet count

### Immunological effects (Section 2.5)

- immunoglobulin and cytokine levels
- WBC, lymphocytes

### Reproductive and developmental (Section 2.6)

- hormone levels
- sperm parameters
- spontaneous abortion/miscarriage
- preterm birth, low birth weight
- malformations, neonatal mortality

### Respiratory effects (Sections 2.7 and 2.8)

- Diffusing capacity
- FEV<sub>1</sub>, FVC, VC
- nonneoplastic lesions in lung
- nasal pathology including ulceration

## Oral

### Cancer

- stomach cancer mortality

- oral, liver, urinary, other GI tract mortality

# Science question 1: Methodological considerations for evaluating epidemiology studies

Methodological characteristics will be considered in EPA's evaluation of hexavalent chromium epidemiology studies, including aspects of the study design affecting the internal or external validity of the results.

EPA is seeking discussion of:

- Additional literature that has a bearing on methodological considerations specific to hexavalent chromium
- Literature relevant to evaluation of exposure measures for populations occupationally-exposed to hexavalent chromium

# **Science Question 2: Inhalation cancer dose-response modeling**

# Lung Cancer Studies, Organized by Setting (Table 2-8)

Baltimore chromate production plant <i>(after improvements to production facilities)</i>	Gibb et al. (2000)
Ohio chromate production plant	Proctor et al. (2004)
Modern production facilities	Birk et al. (2006) Luippold et al. (2005) Industrial Health Foundation (2002) Davies et al. (1991)
Stainless steel welders	Gerin et al. (1993)

## Science question 2: Inhalation cancer dose-response modeling

At the June 2014 IRIS Bimonthly Public Science meeting, we discussed focusing the review of the human lung cancer evidence on studies that might improve the quantitative dose-response analysis of the inhalation cancer data.

EPA is seeking public discussion of:

- Selection of human studies in the lung cancer evidence table
- Issues related to combining data sets in conducting quantitative dose-response modeling