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## HEXAVALENT CHROMIUM

# BASIC Guide: Biomonitoring and Surveillance of Chemical Exposure in Occupational Settings

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CHEMICAL NAME(S): **HEXAVALENT CHROMIUM (CR (VI))**

*EC No. 200-753-7 CAS No. 71-43-2*

| Biomarker(s) | Total Cr (U–Cr) |
|---|---|
| **Biomonitoring triggers** [1] [2] | Especially when hexavalent chromium compounds (Cr(VI)), which are classified as both carcinogenic and respiratory sensitizers, are used, for example in surface treatment activities such as bath plating, or in situations where Cr(VI) fumes may be generated, such as during the manufacturing or welding of stainless steel, or when applying or removing hexavalent-chromium-containing chromates in surfaces, primers, or coatings. |
| **Biological matrix** | Urine |
| **Additional consideration** | Hexavalent chromium readily transforms into trivalent chromium in blood. Therefore, a limitation of this method is that it is a non-specific biomarker, as it does not distinguish between Cr(VI) and Cr(III), and exposure to Cr(III) may influence U-Cr levels. However, U-Cr has been shown to correlate well with airborne Cr(VI) concentrations when individuals are exposed to different hexavalent chromium compounds, for example during surface treatment activities or welding. Exposure levels well below the most stringent OELs are unlikely to cause significant increases in urinary chromium concentrations compared with background levels. Background U-Cr levels in the general population are primarily attributable to exposure to Cr(III), for example through diet, and these levels may vary between countries [1]. |
| **Initial half-life (hours)**[3]<br>i.e., apparent urinary elimination half-life | Urinary total chromium (U-Cr) reflects both recent and past exposure, and may show day-to-day accumulation over the course of the working week.<br>• Welders: U-Cr exhibit a multi-phase elimination process, with reported biological half-lives of approximately 7 hours, 15-30 days, and 3-5 years, respectively [2-5].<br>• Chrome platers: U-Cr demonstrates a biological half-life of approximately 2-3 days [6, 7]. |
| **Type of sample** | Spot Urine |
| **Sampling time** | Workers: Post-shift sample at the end of the working week.<br>Alternatively, paired samples (pre-shift at the start of the working week and post-shift at the end of the working week). Workers should remove their work clothes and thoroughly wash their hands before the urine collection to avoid contamination of the urine sample. |

[1] The strong correlations observed between U-Cr levels and air Cr(VI) in platers and welders support the use of U-Cr as a primary method for the biomonitoring of Cr(VI) exposure at workplaces.
[2] While methods such as red blood cell chromium (RBC-Cr) and exhaled breath condensate chromium (EBC-CrVI/CrIII) have been explored in research settings, they are not currently supported by established guidance values and are offered by only a limited number of laboratories. Despite being presented as potential
[3] Absorption and therefore elimination/excretion of chromium from the body depends on the chromium species and their solubility.

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| **Sampling time after Incidents[4]** | Following a spill or an incident, collect a spot sample from every urine void at time intervals at least up to pre-shift on the next day (when possible). Label each sample with time of collection and time of incident. Exposed worker(s) should not get back to work in the same area with possible Cr exposures till this assessment is going on. |
| **Sample collection at the communtiy level** | Spot urine samples for a sufficiently large population[5]. |
| **Type of container for sample collection from the participants** | Commercially available medical grade plastic containers are preferred (e.g., polystyrene, polypropylene). |
| **Volume of samples** | Recommended minimum of 1 ml for one analysis (duplicate aliquots plus some for creatinine). |
| **Storage and Transportation (according to UN3373 for shipping)** | Samples should be shipped to the laboratory as soon as possible (within 2 days), if not, samples should be refrigerated. |
| **Blank samples or control samples** | • Not required for routine occupational biomonitoirng.<br>• In the case of field study, field blanks should be included in each batch as analyte free water poured into the container in the field. |
| **Sample handling considerations (possibility of contamination and loses)** | For all metals, prevent contamination by using clean, metal-free containers and handling samples with washed hands and gloves. With proper handling and making sure that Vials are sealed properly, contamination and loses are unlikely |
| **Lab Storage** | Short-term storage in the fridge (2-10°C) if to be analysed in under 4 weeks. Frozen at -20°C for longer term storage. |
| **Analytical detection method and laboratory** | ICP-MS (inductively coupled plasma - mass spectrometry) |
| **Method limit of quantification (LOQ)** | Depends on the sensitivity of the analytical method used, the LOQ preferably ≤ 0.1 µg/L. |

[4] It's advisable to develop an action plan and have sample containers ready. For post-incident sampling, it's crucial to record the time and date of collection and gather 3 to 4 spot samples within 24 hours. Not all samples need to be analyzed, but the most appropriate ones can be selected. Often, if there is an incident there will be various actions undertaken (clean-up, removing personnel involved from the scene etc.) and a urinary sample typically will be taken afterwards. So, timing is less critical, especially if multiple samples are collected. This is highly recommended as it will allow to estimate the actual concentrations people have been exposed to.

[5] For cross-sectional studies, spot urine samples, preferably first morning voids could be used. First morning voids are preferable to other spot urine samples since they are collected at about the same time each day for all participants and the results may better correlate with those from 24 h samples (Kissel et al., 2005).

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5. In the laboratory acidification of the samples to a standardised pH of 2 should be considered. The amount of measured SPMA may change as a function both of pH and of storage conditions. An acidic pH leads to the conversion of its precursor, increasing the SPMA metabolite concentration. A study (Paci et al., 2007) showed that a previous hydrolysis procedure can increase SPMA urinary concentrations by factors of up to 5 compared to pH 2 condition and up to 100 when no acid treatment is performed. As urine pH is variable, the hydrolysis at a standardised pH (i.e. 2) is essential to be able to compare results. If the sample is stored at pH of 2 the hydrolysis will proceed, and the analyst must be aware of this.
6. An analytical method with appropriate performance, which is offered by at least one laboratory.

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|---|---|
| **QA/QC procedure at the laboratory** | Quality control and assessment depend on national or local requirements.<br>The selected laboratory should be able to demonstrate that they operate compliant with adequate laboratory quality standard (e.g. ISO 17025, ISO 15189 and GLP).<br>It is recommended that biomonitoring laboratories regularly participate in external QA programs, for instance:<br>G-EQUAS (http://www.g-equas.de/)<br>and follow standards such as<br>Standard Reference Material® 2668 (https://tsapps.nist.gov/srmext/certificates/2668.pdf) |
| **Recommended adjustments** | Measurement of Urinary creatinine concentrations and normalize Cr results to creatinine or alternatively to specific gravity of urine. |
| **Preferred units for expression of results** | • µg Cr/g creatinine when creatinine used for correction<br>• µg Cr/l when results are normalized to specific gravity |
| **Conversion factor** | 1 gram = 0.019232 mole<br>1 mole = 52 gram |
| **Reproducibility of the method (overall coefficient of variation, CV)** | Obtain the report from laboratory regarding reproducibility of the method. The lab report should state their method validation parameters in the report. |

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| Interpretation of results | |
|---|---|
| **Reference values[6] / Background Level (general population level)** | **Check Established Reference Values (RV):**<br>Begin by reviewing reference values that have been established in different countries. If such values are not available, consider using the 95th percentile (P95) from relevant studies as an alternative benchmark. Additionally, consider pre-shift sampling, where applicable.<br>When applying reference values, take into account the **time period** and **geolocation** of sample collection used for their establishment. These factors are critical because reference values may vary due to **temporal trends** or regional differences.<br><br>Examples from specific countries:<br>· Germany: The DFG BAR (representing P95 level in adult general population) is 0.6 µg/L<br>· Finland: 0.3 µg/L (representing P95 level in adult non-occupationally exposed population)<br>· France: 0.65 µg/L (representing P95 level in adult general population)<br>· US (NHANES): 0.99 µg/L (representing P95 level in adult general population)<br><br>See also:<br>• BAuA - Biomonitoring Information System - Federal Institute for Occupational Safety and Health: https://www.baua.de/DE/Themen/Chemikalien-Biostoffe/Gefahrstoffe/Biomonitoring/Biomonitoring-Auskunftssystem<br>• PEH database Personal Exposure and Health Data Platform \| VITO HBM<br><br>**For Smokers: no difference** |

[6] Statistical ranges based on a reference population. Exceeding the reference range doesn't necessarily indicate a health risk but suggests higher exposure than the general population. Sensitivity can be assessed by comparing its LOQ with expected values in the general population and workers, avoid LOQ at the OBL level, aim for LOQ < 10% of OBL with < 50% variability.

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|---|---|
| **Occupational Exposure Limits (OEL) ppm (mg/m³) 8-hour TWA** | Check the international, national and/or company requirements for instance:<br>• GESTIS - International limit values: https://ilv.ifa.dguv.de/limitvalues/4437<br>• SER Grenswaarde (currently not available in English): https://www.ser.nl/nl/thema/arbeidsomstandigheden/grenswaarden-gevaarlijke-stoffen/grenswaarden)<br>• https://pubchem.ncbi.nlm.nih.gov/; Chromium - Hazardous Agents \| Haz-Map<br>• https://echa.europa.eu/indicative-oelvs-directive-2000-39?p_p_id=eucleflegislationlist_WAR_euclefportlet&p_p_lifecycle=0<br><br>In Europe, the binding OEL set under the EU Directive 2004/37/EC is 5 µg/m³ and a process on-going to reduce this value. |
| **Cancer risk threshold** | Lung cancer risk of approx. 4:1000 at 40 years of occupational exposure to 1 µg/m³ of CrVI[7] [8] |
| **Biological limit values (BLV) corresponding to Inhalation Occupational Exposure Limits (OEL) ppm (mg/m³) 8-h TWA** | Check for national requirements or international databases.<br><br>Air level corresponding to different BLV is presented in **Table 1.** |
| **Possible Co-Exposure** | Nickel (Ni) in welding and steel production. |
| **Consideration for selecting biological limit values** | Differentiate between oxides formed under hot conditions, e.g. in welding or manufacturing of for example stainless steel and highly soluble Cr(VI) compounds, e.g. in chromium plating activities. |

[7] https://www.healthcouncil.nl/documents/2016/09/30/hexavalent-chromium-compounds

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***Table 1.*** *Selected Biological limit values (BLV) corresponding to Inhalation Occupational Exposure Limits (OEL) ppm (mg/m³) 8-hour TWA**

| Biomarker(s) | Biological Limit Value (BLV) Finland applicable to applied to all Cr(VI) exposures | | Harmonized PARC value | | ANSES[9] [9, 10] | |
|---|---|---|---|---|---|---|
| | BLV | corr. OEL[a] | HBM GVs | corr. OEL | BLV | corr. OEL |
| **Urine Total Cr (U–Cr) soluble CrVI compounds (e.g. in chrome plating industry)** | 10 µg/L | 5 µg/m$^3$ | 2.7 µg /L | 1 µ g/m$^3$ | 2.5 µ g/l | 1 µg/m$^3$ |
| **Urine Total Cr (U–Cr) less soluble CrVI (oxides) in welding** | 10 µg/L[b] | 5 µg/m$^3$ | 1.4 µg /L | | NA | NA |

[a] *corresponding OEL;*

[b] *Although the value is based on the air Cr(VI) to U-Cr correlations observed in chrome plating, the value has been applied to all Cr(VI) exposures*

**General guidance for reporting results (individual values and aggregated data by SEG)**

Biomonitoring results should be provided to each worker as individual values. Employers receive aggregated results for Similar Exposure Groups (SEGs), which are groups of workers with comparable tasks and exposure. This approach protects individual confidentiality while allowing employers to manage exposure risks effectively. It is recommended in OECD guidelines and Hopf et al. (2024) [11, 12].

[8] *HTP-Arvot 2020 - Haitallisiksi Tunnetut Pitoisuudet, Sosiaali- Ja Terveysministeriön Julkaisuja 2020:24*

[9] *Les valeurs de référence (VR) | Anses - Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail*

*Example of Chromium Compounds*

| Substance | CAS No. | EC No. |
|---|---|---|
| **Chromium trioxide** | 1333-82-0 | 215-607-8 |
| **Chromic acid, oligomers of chromic acid and dichromic acid, dichromic acid** | 7738-94-5; 13530-68-2 | 231-801-5; 236-881-5 |
| **Sodium dichromate** | 7789-12-0; 10588-01-9 | 234-190-3 |
| **Potassium dichromate** | 7778-50-9 | 231-906-6 |
| **Ammonium dichromate** | 7789-9-5 | 232-143-1 |
| **Potassium chromate** | 7789-00-6 | 232-140-5 |
| **Sodium chromate** | 7775-11-3 | 231-889-5 |

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## Revision History

| *Revision Number* | *Date of Change* | *Description of changes* |
|---|---|---|
| Version 1.0 | 2025-12 | Version 1.0 is created |

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