

How to link biomonitoring data to sources of exposure to enable effective risk management?

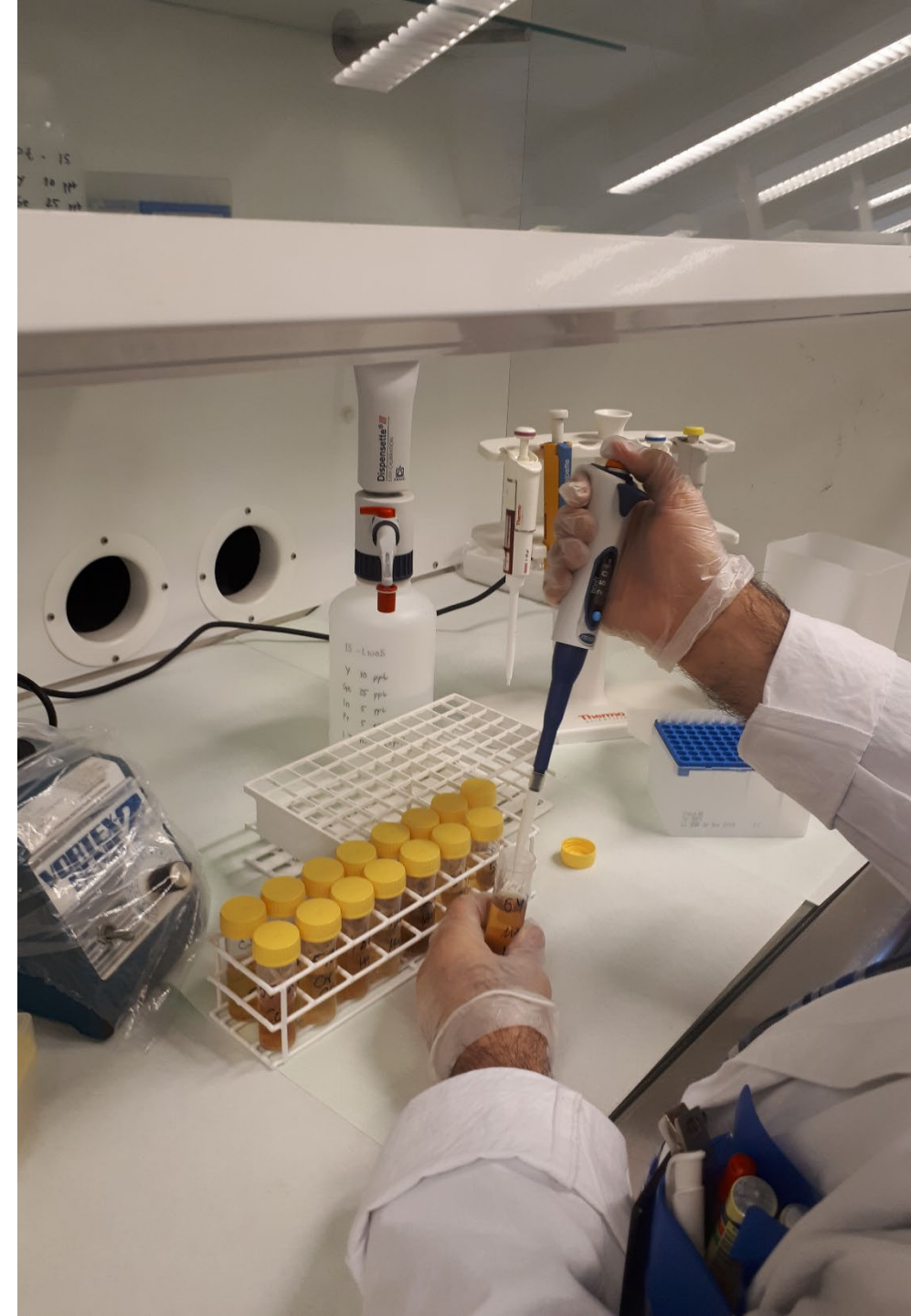
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Biomonitoring as an aggregate exposure assessment tool

- Biomonitoring gives information on the total, aggregate exposure to the chemical of interest
- Benefits:
 - Considers all the sources of exposure (food, environmental, consumer products, occupational)
 - Considers all routes of exposure (including dermal and hands-to-mouth exposure in occupational settings)
 - Considers the impact of personal working habits and personal protection
- Challenges:
 - Identification of the most relevant exposure sources and routes to target risk management measures
 - Linking internal levels to external exposure



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**Inclusion of biomonitoring
generally benefits risk
assessment,
providing it with more
confidence especially when
used together with
other exposure data.**

Santonen et al., 2022, IJHEH, Vol. 249, April
2023, 114139

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Examples from authorisation applications

- Lead chromate:
 - Lead not absorbed through the skin (dermal exposure considered negligible)
 - Inhalation exposure, conservative estimates suggested exposures $< 10 \mu\text{g}/\text{m}^3$
 - However, majority of B-Pb measurements were clearly above general population background levels, and in 30% of cases B-Pb $> 100 \mu\text{g}/\text{l}$



Examples from authorisation applications

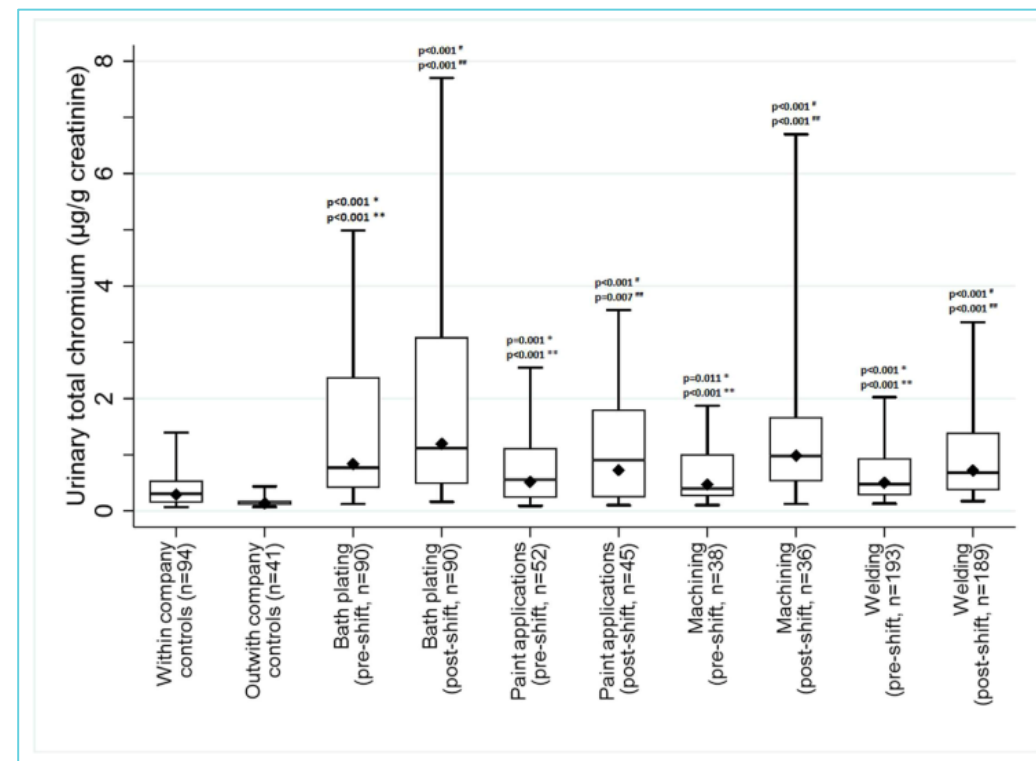
- MOCA (4,4'-methylenebis[2-chloroaniline]):
 - Use in polyurethane manufacturing
 - MOCA has low volatility, but it is well absorbed through the skin
 - In MOCA authorizations, air levels have been generally low but modelling of dermal exposure have suggested dermal exposures up to >10 mg/kg in some contributing scenarios (melting and mixing phases). Assuming 50% dermal absorption this corresponds urinary MOCA levels of >100 $\mu\text{mol/mol}$ crea.
 - Biomonitoring data from the companies shows exposure levels generally well below <10 $\mu\text{mol/mol}$ crea.



CrVI exposure and exposure sources in HBM4EU Chromates Study

- In HBM4EU Chromates study* we observed that the highest internal exposures were related to the use of Cr(VI) in electrolytic bath plating.
- This was regardless of higher air levels measured in paint applications.
- It was also noted that there might be relevant bystander exposure in these industries.

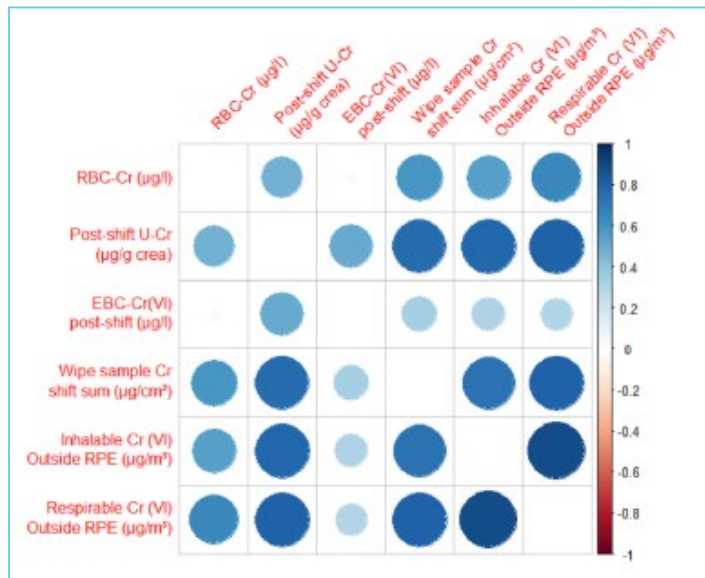
* Santonen T et al., HBM4EU chromates study - Overall results and recommendations for the biomonitoring of occupational exposure to hexavalent chromium. Environ Res. 2022 Mar;204(Pt A):111984. doi: 10.1016/j.envres.2021.111984.



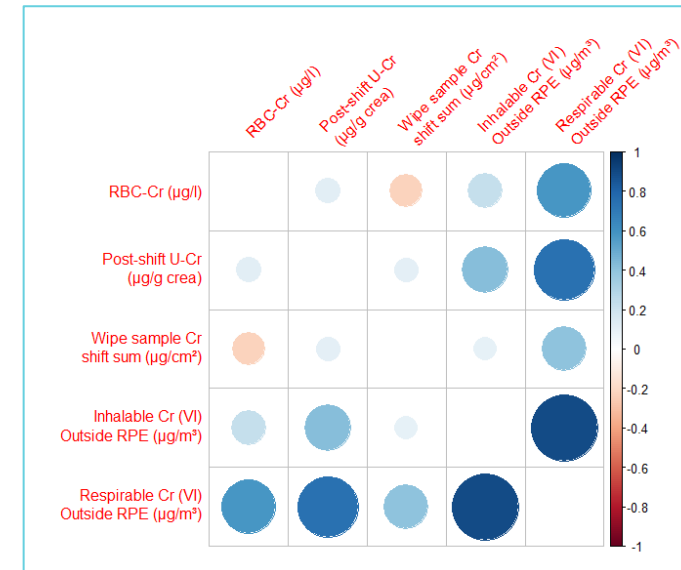
Job title	Inhalable Cr(VI) levels, median; 95 th percentile (n)	Respirable Cr(VI) levels, median; 95 th percentile (n)
Bath plating workers	0.43; 5.13 (57)	0.09; 2.28 (54)
Chromate paint applications	5.61; 154 (7)	n.d.
Machining workers	0.10; 0.41 (15)	0.03; 0.05 (10)
Welders	0.50; 4.06 (107)	0.11; 22.31 (20)
Thermal spraying	9.63; 21.04 (5)	0.06; 0.10 (5)

CrVI exposure and exposure sources in HBM4EU Chromates Study

- In addition to inhalation exposure, dermal contamination showed significant correlation with U-Cr levels in platers but not in welders
- This suggests a potential role of hand-to-mouth behavior to total exposure. On the other hand, wipe sample results correlated also very well with air CrVI levels.



Platers

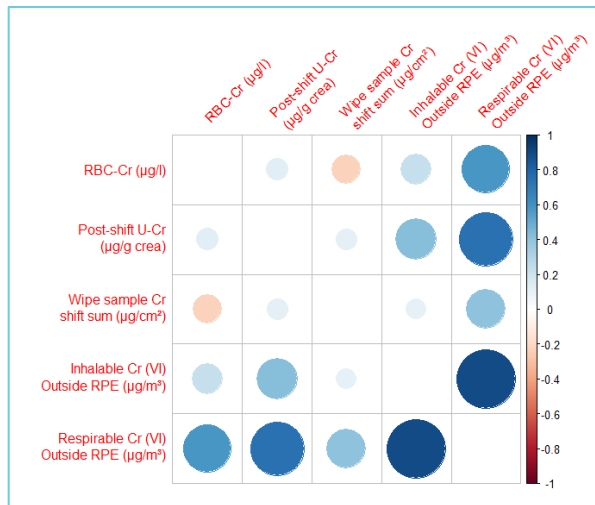


Welders

Welding- exposure routes and correlation between exposure and specific risk management measures

- In welders, the internal exposure correlated with CrVI air levels; the use of local exhaust ventilation (LEV) and respiratory protective equipment (RPE) seemed to be effective in reducing exposure in welding.

Spearman correlations: welders

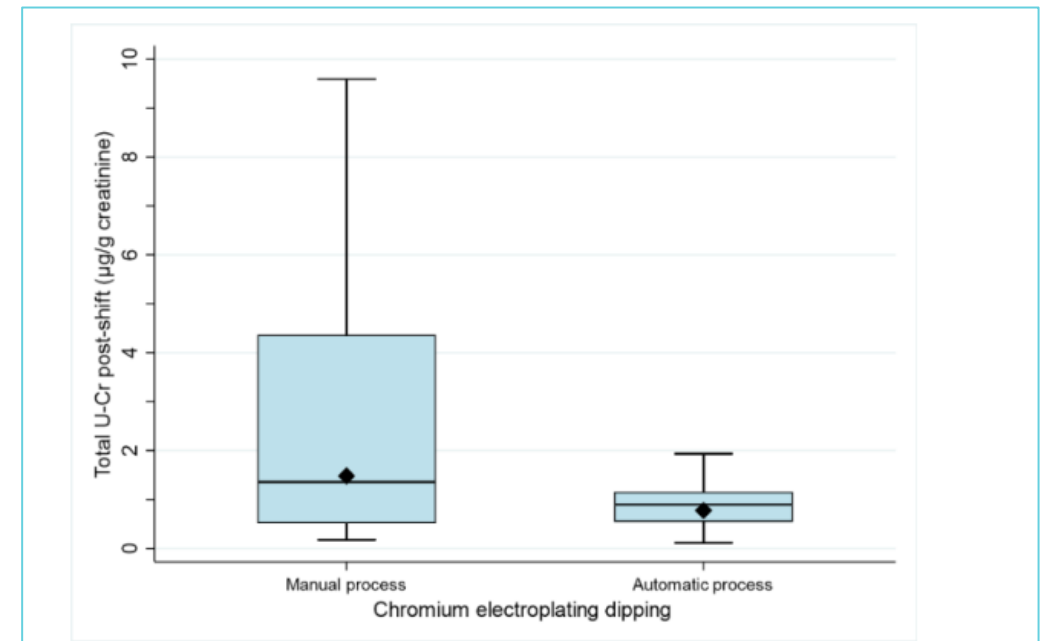


Activity	RMM	Urine Total Cr	Air Inha out-RPE Total Cr	Air Inha out-RPE Cr(VI)	Air Inha in-RPE Cr(VI)	Air Resp out-RPE Cr(VI)	Hand Wipe Total Cr
Welding (n = 195)	Use of RPE	Yes (p = 0.004)	—	—	—	—	—
	Daily fit check of RPE	No	—	—	—	—	—
	Use of gloves	No	—	—	—	—	No
	Availability of LEV	Yes (p = 0.001)	Yes (p = 0.015)	Yes (p < 0.001)	No	No	No
	Dedicated place for storing work clothes	No	—	—	—	—	No
	Dedicated place for storing RPE	No	—	—	—	—	No
	Previous training	Yes (p = 0.010)	—	—	—	—	Yes (p = 0.005)
	Previous monitoring campaigns	Yes (p < 0.001) ^a	No	Yes (p < 0.001) ^b	Yes (p = 0.001) ^b	No	No

Viegas et al., 2022, Int. J. Environ. Res. Public Health 2022, 19, 3683.

Plating - exposure routes and correlation between exposure and specific risk management measures

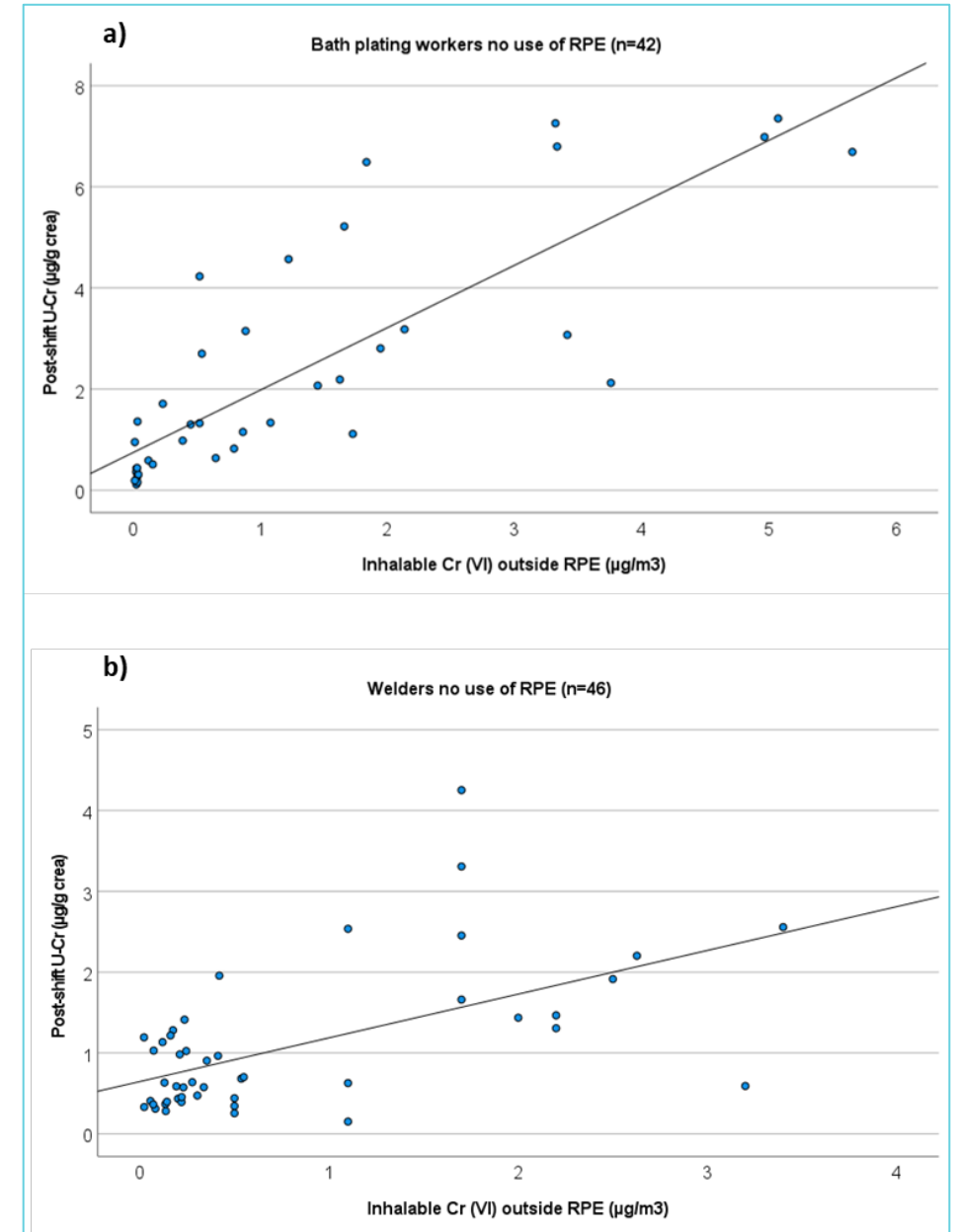
- When evaluating the potential impact of different RMMs on exposure, automation of the process seemed effective in reducing exposure
- Similarly, the use of RPE correlated with lower total exposure
- Based on these results it is not possible to quantitate how much dermal contamination affected total urinary levels but at least they show that attention needs to be paid also to dermal protection and general good industrial hygiene practises in plating activities



Correlation between air CrVI and U-Cr levels

- Even though U-Cr is not specific for Cr(VI), a strong correlation with air Cr(VI) levels in platers was seen.
- Because of the differences in the kinetics of different CrVI species, welding resulted in lower U-Cr levels as plating at the same A-CrVI levels.
- Our regression analyses on the correlations between Air-Cr(VI) levels and U-Cr in platers and welders can be used to set biomonitoring limit/guidance values for U-Cr corresponding air CrVI limit values.

=> If U-Cr levels show clearly higher exposure than predicted by the air levels, this might be due to high dermal exposure.



The use of HBM data in (regulatory) chemical risk assessment

- Within HBM4EU WP5 risk assessment of several HBM4EU priority compounds were performed on the basis of HBM data
- The results have been summarised in Santonen et al., 2022, IJHEH, Vol. 249, April 2023, 114139 together with some methodological aspects and recommendations for the use of HBM data
- Includes examples focusing on both general population and occupational exposures



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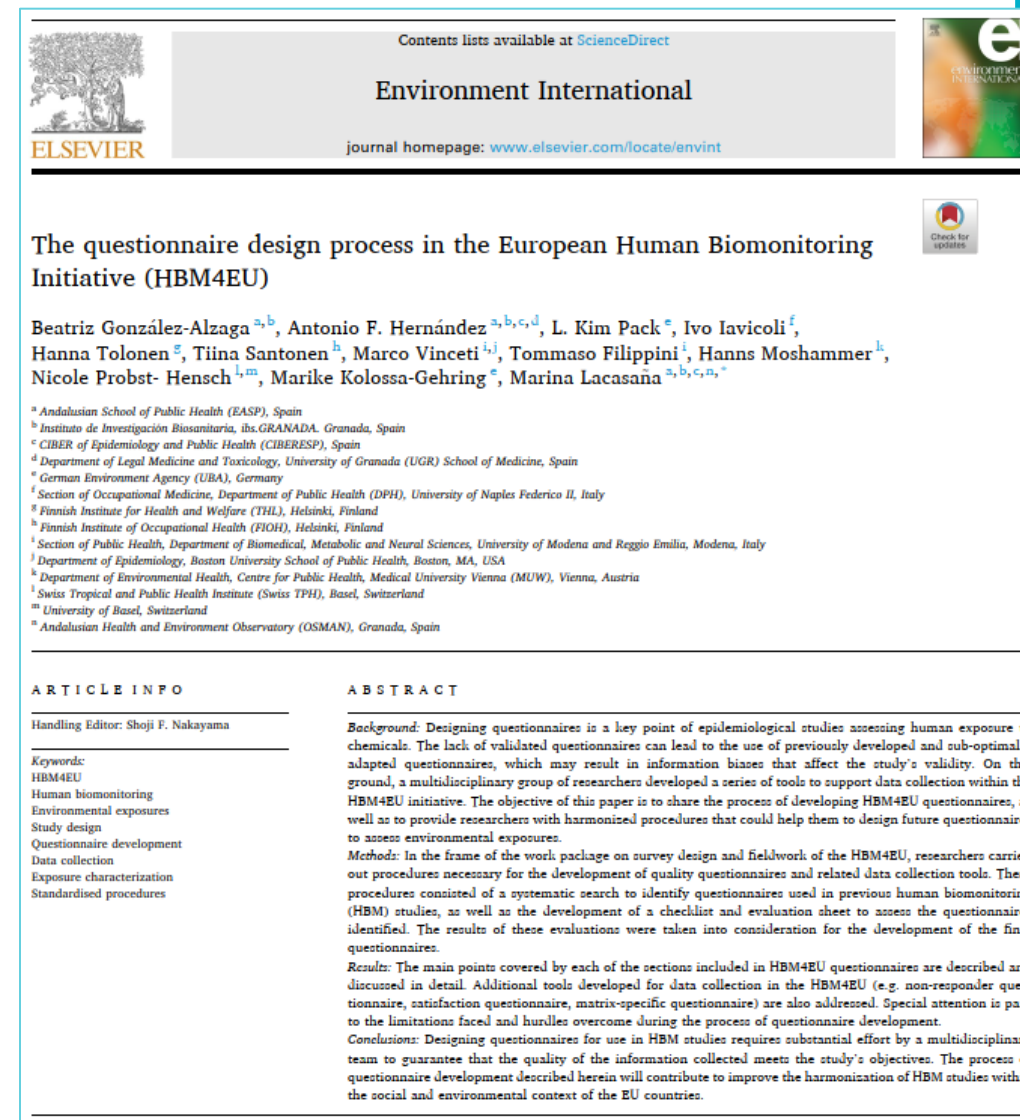
How to use human biomonitoring in chemical risk assessment:
Methodological aspects, recommendations, and lessons learned
from HBM4EU

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The use of HBM data in (regulatory) chemical risk assessment

- In several cases, the use of biomonitoring data for risk assessment was able to confirm the results of the earlier exposure/risk assessments that had used external exposure estimates, reducing the overall uncertainty related to the risk assessment.
- Examples: acrylamide, and UV-filter BP-3
- Either PBPK modelling or simple TK approaches were used to convert internal levels as external exposure

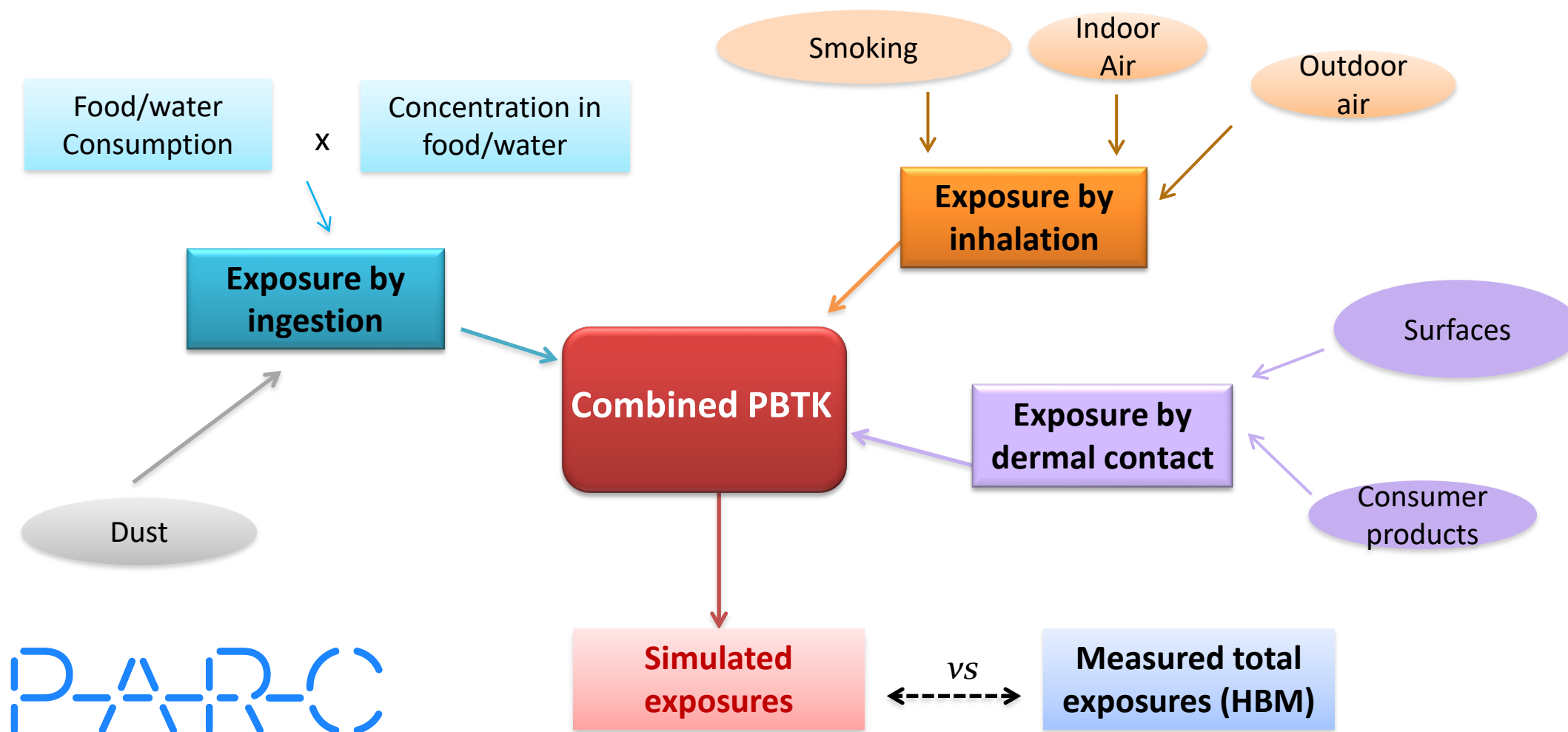


The use of HBM data in (regulatory) chemical risk assessment

- HBM is generally extremely beneficial in cases when exposure sources are multiple and/or substance is cumulative
 - Examples phthalates, PFAS
- Questionnaires focusing on potential exposure determinants may bring additional information on the most relevant exposure sources in these cases
- Repeated HBM studies e.g. in case of phthalates bring information on the impact of specific regulatory measures on total exposure



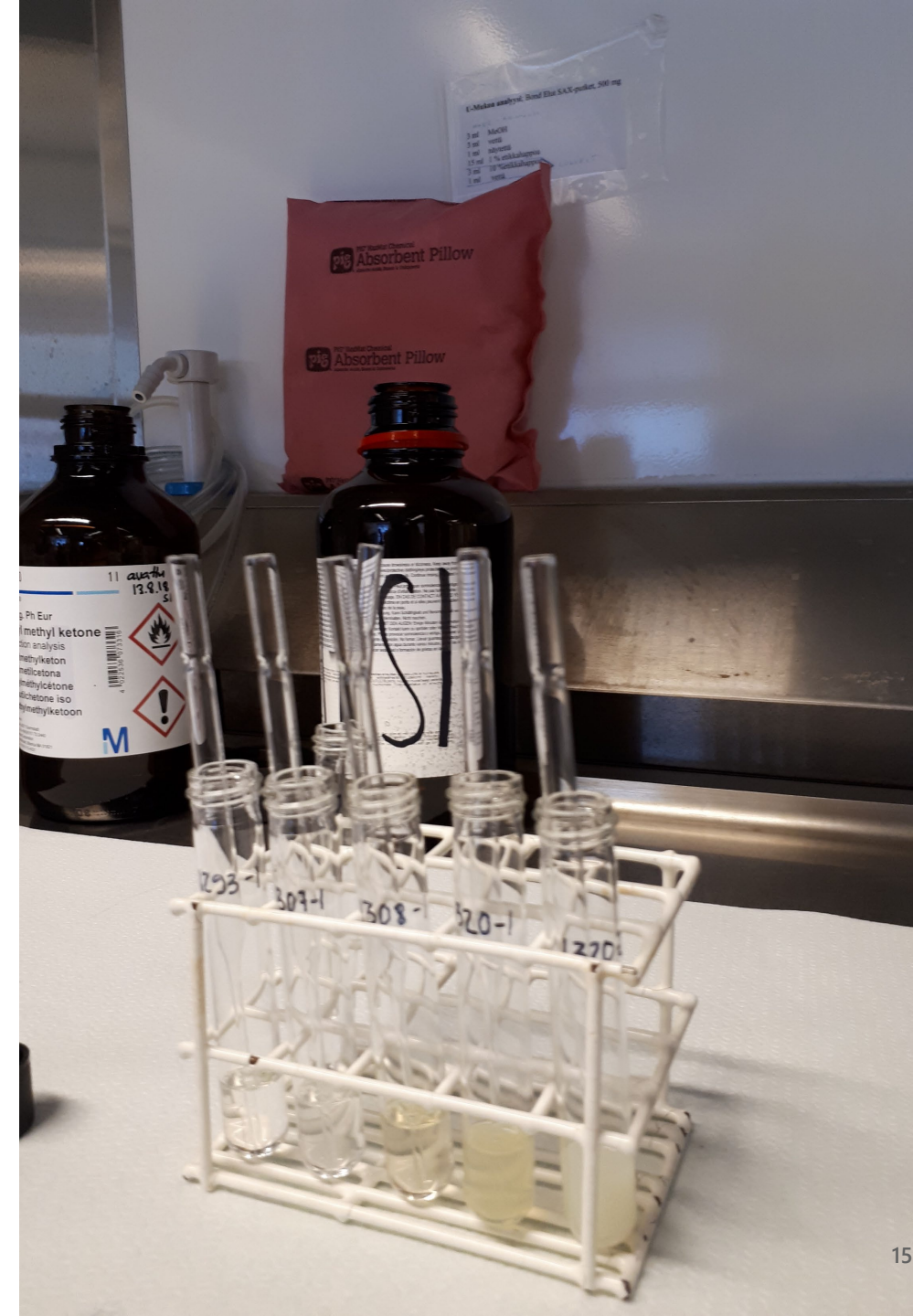
PARC T6.2.1 on aggregated exposure



PARC

Summary

- Biomonitoring gives information on aggregated total exposure
- Integrating HBM data to other information is often needed to identify the main exposure sources, allowing targeting of risk management measures.
- Biomonitoring is extremely useful as a “reality check” for exposure estimates made based on external exposure and modelling.



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