



HBM4EU Rapid Response Mechanism (RRM): HBM aggregated data on copper

KEY FINDINGS

- The HBM4EU **Rapid Response Mechanism (RRM)** allows policy makers at national and European levels to submit requests for specific information to the HBM4EU Consortium.
- The RRM is of particular importance to **reduce the gap between science and policy**, especially for substances that have not been prioritised according to the chemical prioritisation strategy elaborated in the project.
- The first request was for aggregated HBM data for **copper (Cu)** to support the renewal of approval of **Cu compounds as active substances for plant protection products (PPP)**.
- HBM4EU's consortium successfully gathered aggregated HBM data on Cu from **35 data collections** of **13 different countries across Europe**, collected from **HBM4EU National Hubs** or directly from **data owners**.
- A generic PBTK (physiologically-based toxicokinetic) model was adapted to model the complex **toxicokinetics** associated with **lifelong exposure** of the general population.

WHY A RAPID RESPONSE MECHANISM?

The RRM allows policy makers at national and European levels to submit to the HBM4EU Consortium requests for specific information. Thus, the RRM is open to the National Hub Contact Points of HBM4EU countries' members, as well as to members of the European Union Policy Board, via the HBM4EU website¹.

The **aim** is to **ensure that HBM4EU can respond to new and urgent needs for information in the EU and national policy community** regarding human exposure to substances, outside of the formal timeframes for nominating substances (described in Ougier et al, (2021)²).



¹ <https://www.hbm4eu.eu/rapid-response-mechanism/>

² Ougier E, Ganzleben C, Lecoq P, Bessems J, David M, Schoeters G, Lange R, Meslin M, Uhl M, Kolossa-Gehring M, Rousselle C, Lobo Vicente J. (2021). [Chemical prioritisation strategy in the European Human Biomonitoring Initiative \(HBM4EU\) – Development and results](#). Int J Hyg Environ Health 236:113778.



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FIRST REQUEST ADDRESSED: COPPER EXPOSURE CASE-STUDY

In October 2018, **DG Health and Food Safety** submitted to HBM4EU an urgent request for information related to Cu compounds, via the online RRM.

This request related to the renewal of approval of Cu compounds as active substances for **plant protection products (PPP)**.

HBM4EU was requested to assess HBM data and to establish whether:

- All these Cu compounds are similarly absorbed and excreted;
- Cu compounds used as plant protection products are more contributing to the human body burden of Cu than other sources;
- Cumulative exposure assessment can realistically bring an added-value to the risk assessment of Cu.

ANALYSIS OF DATA COLLECTED ACROSS THE CONSORTIUM

The mobilisation of the consortium to gather aggregated HBM data was a success with **35 HBM data collections** providing aggregated data on Cu from **13 different EU countries**, collected from **HBM4EU National Hubs** or **data owners**. Among those 35 data collections, all of Europe regions were represented: 16 came from Western Europe, 13 from Southern Europe, 5 from Northern Europe and 1 from Eastern Europe (Figure 1).

Figure 1: Countries for which HBM aggregated data on Cu were provided.

35 HBM data collections from 13 countries:

- 16 from Western-Europe
- 13 from Southern-Europe
- 5 from Northern-Europe
- 1 from Eastern-Europe



The HBM data were aggregated data for the whole study population, or stratified for age, sex, body mass index (BMI) and smoking status. As there were many **differences between the data collections** (e.g. blood matrix, urine sampling types, pregnancy, age), a relatively small number of data collections per stratifier was reported, implying that care should be taken not to over-interpret the data. Most data collections reported results for total Cu in blood and urinary results were reported only in 17 of them.



USE OF A GENERIC PBTK MODEL TO MODEL THE KINETICS OF COPPER AND COPPER COMPOUNDS

Copper in blood is tightly regulated by **homeostatic mechanisms**. The generic PBTK model of the **INTEGRA** platform has been used to model Cu homeostase for integrated internal exposure assessment.

The generic PBTK model as parameterised for Cu was able to describe its toxicokinetic behaviour for a lifelong exposure of the general population and has shown its capacity to capture Cu homeostasis under real life intake patterns.

Additional exposure and toxicokinetics data are needed to cover shorter but at the same time higher exposure patterns related to occupational exposure to explain how they may affect Cu homeostasis. As it seems that long-term Cu intake levels are reflected to some extent in the overall body burden, detailed information about the **dietary intake** or **exposure through other routes** is also needed to explain the differences observed in the blood Cu levels in the HBM cohorts that were available.

CONCLUSION

Despite the need for additional data, the results were of interest to DG Health and Food Safety and the European Food Safety Authority (EFSA) in different ongoing tasks on Cu (setting of an updated health-based guidance value, re-evaluation of Cu compounds in plant protection products and activities regarding Cu as nutrient feed additive). Still, this first assessment confirmed the necessity to follow up the risk assessment for copper compounds and a mandate was therefore addressed to EFSA to re-evaluate the exposure assessment from all sources of copper, helping to prepare the grounds for the re-assessment of these important fungicidal/bactericidal pesticides very commonly used by farmers, especially in organic farming scheme. This outcome highlights the value and importance to have such a mechanism to reduce the gap between science and policy, especially for substances that have not been prioritised according to the strategy elaborated in the HBM4EU project. Importantly, such a mechanism requires a proper problem formulation stage to well understand the request and its context. This should allow for a clear definition of the research activities to be undertaken by the consortium, to address the request in a most effective way considering the available resources.

More information is available on the HBM4EU website:
[HBM4EU response document to the DG SANTE request](#)