HBM4EU science and policy for a healthy future

HORIZON2020 Programme
Contract No. 733032 HBM4EU

Templates for the submission of urgent requests for new information, one for EU policy makers and one for national policy makers

Deliverable Report

D 4.1

WP 4 - Prioritisation and input to the Annual Work Plan

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2 Work Package 4: Prioritisation and input to the Annual Work Plan

Key objectives of the work package (WP) 4 include:

- Establishing an open dialogue with the potential users of HBM4EU in the policy making community and the related research community, as well as with lay persons, in order to appropriately frame our activities ex ante;
- Mapping the information needs of policy makers at both EU and national levels with regards to human exposure to chemicals and resulting health impacts;
- Developing a prioritisation strategy, to include a set of clear decision-making criteria by which to prioritize substances or groups of substances to address with targeted activities under the WPs;
- Combine policy questions with research needs and draft scoping documents, to feed into the Annual Work Plan (AWP)
- Operate a rapid response mechanism to allow HBM4EU to respond to urgent information requests from policy makers.

3 Task 4.3: Rapid response mechanism

3.1 Objectives

In order to respond to new and urgent needs for information in the EU policy community and at national level, a rapid response mechanism will allow policy makers to submit requests for specific information. These information requests may require new surveys on particular chemicals or in particular geographical regions (respecting the scope of countries included in the HBM4EU consortium), or may focus on specific vulnerable groups. Alternatively, requests may require the development of new research activities, or new approaches to data analysis of existing data.

3.2 Rapid response mechanism procedure

A template for the submission of urgent requests for new information should be made available on the HBM4EU website. Authorized applicants should be either EU policy makers or national policy makers. Applicants will be asked to provide as much information as possible against prioritisation criteria established under Task 4.2, in order to allow for an informed assessment of the policy need, as well as the technical and economic feasibility of the activities required to meet request.

ANSES will handle urgent requests for new information, to be submitted via a specific email address.

3.2.1 EU policy makers

The process of the rapid response mechanism for requests from EU policy makers is shown in Figure 1 below:

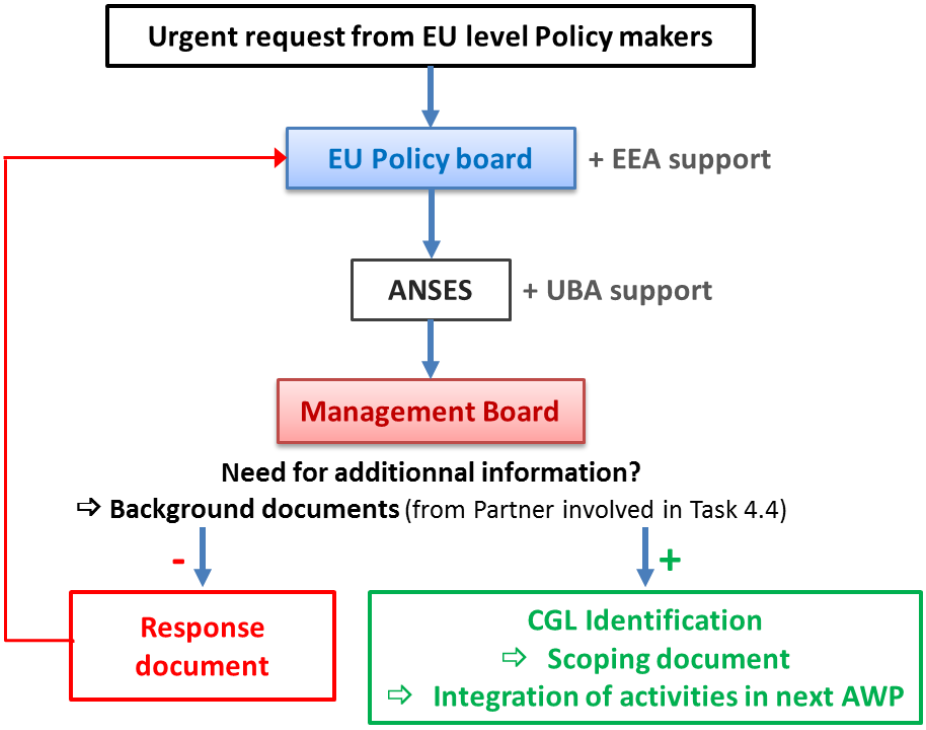


Figure 1 - Rapid respond mechanism procedure for requests from EU policy makers

***ANSES**: Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail ; **AWP**: Annual Work plan ; **CGL** : Chemical Group Leader ; **EEA**: European Environment Agency ; **EU**: European union ; **UBA**: Umweltbundesamt*

Policy requests from the EU level will be channeled through the EU Policy Board to ANSES, with support from EEA. With support from UBA, ANSES will channel all requests to the Management Board in a timely fashion for assessment. With regards to requests from EU level, the Management Board will review the request against the prioritisation criteria generated under Task 4.2. Where additional information is required, a partner with relevant expertise will be requested to produce a background document to support decision making, drawing primarily on the information submitted with the request. The Management Board will decide whether or not to respond to the request by pursuing relevant research under HBM4EU.

Where the decision is positive, the EU Policy Board will be informed and provided with a proposed response. It is expected that request may involve two responses. A first step will be to mobilize the expertise in the HBM4EU Consortium and identify existing evidence that might address the request for additional knowledge. In some cases, this action may be sufficient to respond to the request.

Where this is not sufficient, the second and more resource intensive response will be to identify new research activities to be undertaken under HBM4EU in order to fill a gap in the currently available evidence. Relevant research activities will then be proposed. For a new chemical, a Chemical Group Leader (CGL) will be identified and will proceed with producing a scoping document (Task 4.4), including proposed activities. Should the request concern an existing priority chemical and suggest a particular analysis, such as on a specific vulnerable group, the existing CGL will then integrate the activities into the existing scoping document for that substance. These activities will then be integrated into the next AWP to be developed.

Where the decision is negative, a response document will be produced explaining the rationale behind the decision making.

The time limit for the Management Board decision making process on whether to proceed with acting on a request was initially set at 2 working months. This timespan might be too short, depending on whether the Management Board wishes to make decision during the meetings occurring every 2-3 months. This point should be addressed to the Management Board (see paragraph 5.2). The applicant will be informed of the decision of the Management Board no later than 10 working days after the decision has been taken. In the case of a decision not to act on the request, the applicant will be provided with the response document. The Governing Board, the Stakeholder Forum, the NHCPs and the Advisory Board will be advised of the request and the decision.

3.2.2 National policy makers

The procedure for addressing rapid requests from National Hub Contact Points will be the same as that applied to EU level requests. On receiving the request, ANSES will channel the information to the Management Board. Where additional information is required, a partner with relevant expertise will be requested to produce a background document to support decision making. The Management Board will decide whether and how to respond to the request, as described above.

The National Hub Contact Point will be informed of the decision of the Management Board, through the National Hub Coordinator (NHC), as shown on the Figure 2 below:

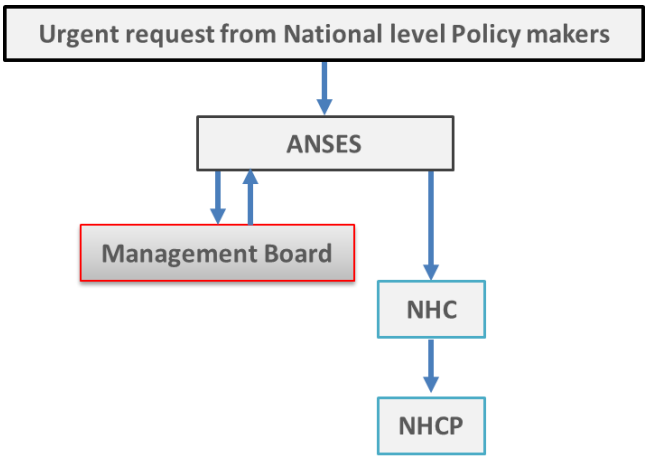


Figure 2 - Rapid respond mechanism procedure for request from National policy makers

***ANSES**: Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail : **NHC**: National Hub Coordinator ; **NHCP**: National Hub Contact Point*

This suggestion for a procedure has been submitted to the Management Board for approval.

3.3 Methodology

The terms indicated in the template should match as much as possible the prioritisation criteria established under Task 4.2 under development, in order to allow for an informed assessment of the policy need, as well as the technical and economic feasibility of the activities required to meet the request.

The template for submission of urgent requests for new information was therefore developed in parallel to Task 4.2 'Prioritisation strategy', for which ANSES is also the Task Leader.

ANSES approach to perform the 4.2 exercise is described hereafter:

- Review of the scientific literature on SCOPUS and Pubmed databases regarding existing methods and strategies on the prioritisation of chemical substances
- Identification of prioritisation criteria

- Selection of criteria that capture scientific evidence, regulatory demands, societal concerns and technical aspects
- Grouping of the selected criteria into categories of criteria
- Suggestion of answer terms (indicators) for each selected criteria

The method applied as well as an Excel spreadsheet including the categories of criteria, selected criteria, sub-criteria and their corresponding indicators was discussed with the partners involved in Task 4.2 (UBA, VITO, AUTH, FIOH, FOEN, IRAS, EAA, NIJZ, EEA, AGES, INSA and DH). A teleconference with the partners involved was organized on 15 March 2017, to discuss the criteria and overall strategy. The proposed prioritisation strategy and criteria were then revised to reflect feedback from the different partners. The prioritisation strategy and criteria draft document will be presented to the EU Policy Board on 28 April 2017. At a later stage, feedback from the Advisory Board and from the Stakeholder Forum is also expected, which possibly will have some influence on the template developed in the Task 4.3.

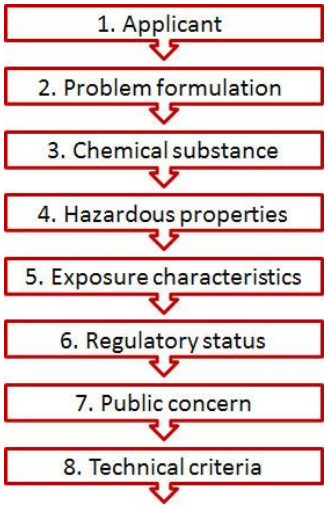
The template for submission of urgent requests for information was developed considering inter alia two aspects:

- the technical collection and processing of the data
- the need to help the applicant defining as specifically as possible his/her request, while also bringing enough elements to have a clear picture of the context in which a knowledge gap is identified

Close-ended questions are therefore included in the template, because they are easier to handle for the web developer (coding) and also for the applicant in terms of data entry. Open-ended questions are also included in the template, in order to encourage the applicants to formulate explicitly their request, thus highlighting the relevance to engage actions.

4 Template

The template is divided into 8 sections.



The applicants are requested to complete all sections and answer as many questions as possible to enable an informed assessment of the policy needs by the MB:

- Tooltips may appear in overprint during the passage of the timekeeper of the mouse on certain elements of the request form
  (text of the tooltips are in Appendix of this report)
- A Guidance manual will also be available on the HBM4EU website (currently under preparation)

Visuals presenting the sections of the template that the applicant will have to fill in are provided hereby for each of the sections hereafter, with the following pictograms:

xxx Free text field

☑ Checkbox field

Date time

Tooltip (definition of acronyms, description of criteria, etc.)

4.1 Section 1: Applicant identification

Applicants should provide contact details, *e.g.* name, telephone number, email, etc., in order to identify themselves and to allow further communication with them.

Who can apply?

- EU policy makers
- National policy makers

➢ **Applicant**		
Applicant	Last name	xxx
	First name	xxx
Institution		xxx
Country		xxx
Telephone		xxx
Email		xxx@xxx
Date of completion		

4.2 Section 2: Problem formulation & aim of request

The applicant is requested to provide background explanation/justification to his/her request with:

- free-text data (description of the context and aim of the request)
- multiple-choice answers

According to the objectives of task 4.3, urgent requests may deal with the lack of (specific) information and/or knowledge needs, requiring „*new surveys on particular chemicals or in particular geographical regions (respected the scope of countries included in the HBM4EU consortium), or it may focus on specific vulnerable groups. Alternatively, requests may require the development of new research activities, or new approaches to data analysis of existing data*“.

➢ **Problem formulation & aim of request**		
Problem formulation and aim of request		xxx
Specific requests	New survey/data on a particular chemical or a group of chemicals	☑
	New survey/data in particular geographical regions	☑
	New survey/data concerning specific target population or subgroups of population	☑
	New data concerning the development of new research activities	☑
	New approaches to data analysis of existing data	☑
	Other request	☑
Please complete with available information and identify any specific knowledge need		

4.3 Section 3: Chemical substance identification

The European Union's 7th Environmental Action Programme sets the goal of assessing and minimizing risks to the environment and health associated with „*hazardous substances*" (including chemicals in products) by 2020.

Which substance?

The chemicals are used in a large range of goods (products) and services that support our lifestyles and economies. Many substances can also be found in our environment including occupational settings.

The applicant is requested to identify the substance of interest by its CAS Registry Number and/or its EC Number and/or by a wide variety of synonyms.

If needed the applicant may choose to highlight a specific concern regarding:

- a chemical group, to be specified in a free-text data field. The feasibility of developing specific questions for chemical groups needs to be investigated within the scope of tasks 4.2 and 4.3. Another option would be either to ask the applicant to complete a template for each of the substances of concern within the identified group of chemicals or ask the applicant to fill in the template with the data on a 'leader' substance of the chemical group and, if possible, to specify whether the other substances within the group seem to have or not the same properties.
- chemical mixtures, with either identified or unidentified substances. Should the substances be identified, completion of a template for each one of the substances may be requested. Should the substances be unidentified, completion of section 5 on the exposure characteristics will be requested.

➢ Chemical Substance(s)		
Single substance		
Scientific name		xxx
CAS number		xxx
EC number		xxx
Other name(s)		xxx
Multiple substances		
Chemical group		xxx
Mixture	Identified substances	☑
	Unidentified substances	☑
Please complete with available information		

4.4 Section 4: Hazardous properties

The use of many toxic or hazardous substances (*e.g.* lead, cadmium, mercury, etc.) is regulated in the European Union: e.g. the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), the Classification, Labelling and Packaging (CLP) regulations are aimed to provide baseline protection for human health and for the environment.

➢ **Hazardous properties**		
Effect	*Classification*	*Indicator(s)*
Carcinogenic	IARC classification	1, 2A, 2B, 3 or 4
	CLP classification	1A, 1B or 2
	Knowledge gap	☑
Mutagenic	CLP classification	1A, 1B or 2
	Knowledge gap	☑
Reprotoxic	CLP classification	1A, 1B or 2
	Knowledge gap	☑
Specific Target Organ Toxicity (STOT)	Single exposure (STOT-SE)	1, 2 or 3
	Knowledge gap	☑
	Repeated exposure (STOT-RE)	1 or 2
	Knowledge gap	☑
Neurotoxicity		Yes, no or suspected
Immunotoxicity		Yes, no or suspected
Respiratory sensitization		Yes, no or suspected
Endocrine disruptor		Yes, no or suspected
Other specific hazardous properties	SVHC	Yes, no, under review or unknown
	Other classification(s)	xxx
	Emerging substance	xxx
Please complete with available information and identify any specific knowledge need ***+ add file(s)***		

4.5 Section 5: Exposure characteristics

This section is aimed to investigate how exposure to the chemical of interest (or possibly a group of chemicals if so indicated here above) affects the health of different target groups or sub-groups.

➢ **Exposure characteristics**		
Criteria	*Sub criteria*	*Indicator(s)*
Extent of exposure	Geographical extent	Hotspots
		Regional
		Country (one or several)
		EU wide
		Unknown
	Duration of exposure	Acute
		Subchronic
		Chronic
		Unknown
	Level of environmental release (E-PRTR)	xxx
	Multisource exposure	Yes, no or suspected
Media of exposure	Air	Yes, no or suspected
	Water	Yes, no or suspected
	Food	Yes, no or suspected
	Soil	Yes, no or suspected
	Products (e.g. cosmetics, etc.)	Yes, no or suspected
	Other	xxx
	Knowledge gap regarding the external exposure	Yes/no
Exposure routes	Dermal	☑
	Inhalation	☑
	Oral	☑
	Trans placental	☑
Prevalence of exposure		Widespread use by workers
		Consumer use
		Unknown
Evidence of exposure from biomonitoring data	Availability of biomonitoring data	Yes/no – add references
Persistence and Bioaccumulation potential	PBT	Yes, no, under review or knowledge gap
	vPvB	Yes, no, under review or knowledge gap
Source of exposure	Natural	Yes, no or suspected
	Anthropogenic	Yes, no or suspected
Volume of production	ECHA database	0-10 tonnes *per annum*
		10-100 tonnes *per annum*
		100-1000 tonnes *per annum*
		>1000 tonnes *per annum*
		Unknown

Target population – High exposed groups	Newborn/children	☑
	Adults	☑
	Pregnancy	☑
	Elderly	☑
	Workers	☑
	Male	☑
	Female	☑
	Other group(s)	☑
Vulnerability	Sex	Yes/no – If « yes » (suspected), please indicate "male" or "female"
	Age	Yes/no– If « yes » (suspected), please complete with available information
	Social classes	Yes/no– If « yes » (suspected), please complete with available information
Please complete with available information and identify any specific knowledge need ***+ add file(s)***		

4.6 Section 6: Regulatory status

With the aim of harmonizing procedures for human biomonitoring across the 26 participating countries, some existing policies relating to the chemicals might be limited in scope. This section seeks to provide information on existing regulations aiming to reduce the health impact of the chemical of interest (or possibly the group of chemicals if so indicated here above).

➢ **Regulatory status**		
Criteria		*Indicator(s)*
Regulation(s)	Legal framework to regulate chemical in EU	Yes/no – add references
	Legal framework to regulate chemical at national level	Yes/no – add references
	Regulatory gap	Yes/no – add justification
Effectiveness of current environmental policy development and implementation	Environmental policy monitoring	Yes/no – add references
Effectiveness of current measures to minimize exposure to the substance or chemical group	Health policy monitoring	Yes/no – add references
Guidance values	Availability of a toxicity reference value	Yes/no – add references
	Biomonitoring guidance values	Yes/no – add references
	Availability of biomarker level in a reference population	Yes/no – add references
	Health impact or risk assessment	Title(s) + link(s)
Potential for exposure prevention or reduction	Human exposure from environmental sources (including products)	Title(s) + link(s)
	Occupational exposure	Title(s) + link(s)
Please complete with available information and identify any specific knowledge need ***+ add file (s)***		

4.7 Section 7: Public concern

This section aims to reflect the level of public concern towards the exposure to the chemical of interest (or possibly to the group of chemicals if so indicated here above) and its potential effects.

➢ **Public concern/social perception**		
		Indicator(s)
Social perception and attitudes towards the substance or chemical group	Available data (surveys, *e.g.* Eurobarometers, etc.)	Title(s) + link(s)
	Lists (e.g. SIN List from Chemsec, NGO)	Title(s) + link(s)
Public information & knowledge	Media coverage	Yes/no or unknown
Please complete with available information and identify any specific knowledge need ***+ add file (s)***		

4.8 Section 8: Technical criteria

This section focuses on the needs to better utilize knowledge regarding the chemical of interest (or possibly the group of chemicals if so indicated here above) and to benefit from:

- Existing expertise on human biomonitoring
- Capacity building

➢ **Technical criteria**		
Criteria		*Indicator(s)*
Biomarker(s)		
Availability	Status	Available & used for HBM
		Available & used for research
		Not available – research need
Analytical method		
Availability	Status	Available & used for HBM
		Available & used for research
		In development but not yet implemented
		Not yet developed – research need
Performance	Estimated additional analytical effort needed	Not necessary
		Minor adaptation from existing methodological basis
		Major adaptation
		De novo development
Please complete with available information and identify any specific knowledge need ***+ add file (s)***		

4.9 Guidance manual (in preparation)

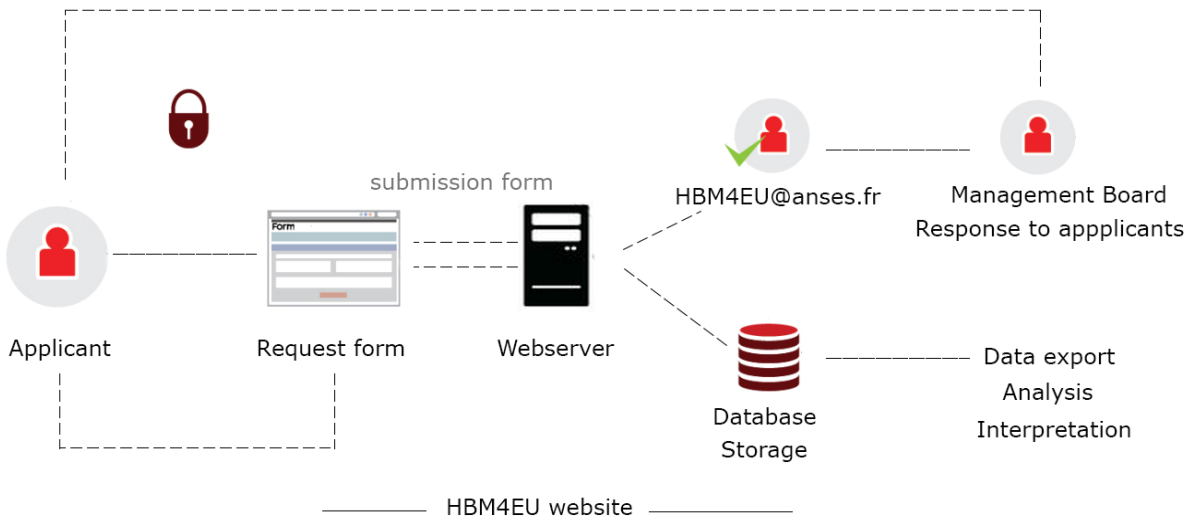
To be expected by July 2017.

5 Points for discussion

5.1 Questions for the web developer

The following technical questions should be submitted to the web developer in connection with the HBM4EU website development:

- What will be the access pathway and the applicant registration mechanism (*e.g.* internal pages, login)?
- How to ensure that the applicant will have the possibility of modifying, completing or reviewing his urgent request before final validation, without losing any previous information? How to ensure the safeguard of the information?
- Once recorded, can the applicant have an indicative dashboard to save, protect and memorize his steps?
- What kind of response page will the applicant get when submitting the request? How to give a registration number?
- How can files be added to the urgent request? How many files and which size?
- Error message: what if something wrong occurs?
- Data export to XLS or CSV from the website database to ANSES?



These technical questions will be discussed in a meeting planned with the HBM4EU web team in April 2017.

Contact in charge of the website: Catherine Ganzleben (EEA)

5.2 Questions for the Management Board

- Does the Management Board consider that 2 working months is sufficient to make a decision on whether to respond or not to the request by pursuing relevant research under HBM4EU?
- Should activities to be engaged in order to respond to urgent requests be included in the forthcoming AWP only if the request is submitted before Month 6 of the year, (i.e. before forthcoming AWP approval by the Management Board)?
- Who has the right to access the template page (EU policy makers, national policy makers, NHCPs, etc.)?
- How about having one template (for EU policy makers and national policy makers) instead of two distinct templates?
- Can the process applied to urgent request from National policy makers be identical to that from the EU policy makers?
- Should the review procedure by the Management Board be identical to that applied to requests from the EU Policy Board?

6 Timetable for the next steps

Task Process	Schedule & deadlines
ANSES submits Deliverable 4.1 to UBA	**7th of April**
Telephone meeting between ANSES, UBA, EEA and the webpage developer to clarify technical aspects of the process for submitting rapid requests online	April 2017

Consults the EU Policy Board on the prioritisation strategy and criteria and the rapid response mechanism	**28th April 2017**
Consult the HBM4EU Management Board on the rapid request mechanism	4th May 2017
Development of the webpages for the rapid request mechanism on the HBM4EU website	July-August
Testing the rapid response mechanism to ensure smooth technical function and user experience	September 2017
Rapid response mechanism in place	**October 2017**

Appendix

The tooltips, which will be appearing on the template, are meant to provide assistance to the user by defining terms (like acronyms), explaining the meaning of some criteria and/or proposing hyperlinks as possible sources of information. Currently established tooltips are described below, according to the different sections.

Section 3: Chemical substance identification

- **CAS Number (Chemical Abstracts Service Registry Number)**: unique numerical identifier assigned to every chemical substance. CAS Numbers are up to 10 digits long using the format [xxxxxxx-yy-z]. See http://www.cas.org

- **EC number (European Community number)**: official unique numerical identifier for chemical substances on the market within the European Union (i.e. European INventory of Existing Commercial chemical Substances (EINECS), European LIst of Notified Chemical Substances (ELINCS) or No-Longer Polymers (NLP)). EC numbers are 7 digits long according to the pattern [xxx-xxx-x]. See https://echa.europa.eu/

Section 4: Hazardous properties

- **Carcinogenic**: ability of inducing tumours, increase tumour incidence and/or malignancy or shorten the time to tumour occurrence

- **IARC (International Agency for Research on Cancer) classification**: Group 1: carcinogenic to humans; Group 2A: probably carcinogenic to humans; Group 2B: possibly carcinogenic to humans; Group3: not classifiable as to its carcinogenicity to humans; Group 4: probably not carcinogenic to humans. See http://monographs.iarc.fr/ENG/Classification/index.php/

- **CLP (Classification Labelling and Packaging) classification:** Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures, introduced on the basis of the United Nations Globally Harmonised System (GHS). See Carcinogenic Mutagenic and Reprotoxic (CMR) categories from Annex IV of the CLP regulation: 1A (known to have CMR potential for humans, based largely on human evidence), 1B (presumed to have CMR potential for humans, based largely on experimental animal data) and 2 (suspected to have CMR potential for humans) on https://echa.europa.eu/regulations/clp/classification

- **Mutagenic:** ability of causing a mutation, which is a permanent change in the genetic material of a cell or microorganism. See ECHA infocards on substances: https://echa.europa.eu/information-on-chemicals

- **Reprotoxic:** ability of causing adverse effects on the reproduction and the reproductive system in animals or humans. ECHA infocards on substances: https://echa.europa.eu/information-on-chemicals

- **STOT (Specific Target Organ Toxicity)**: most substances producing systemic toxicity do not cause a similar degree of toxicity in all organs but usually produce the major toxicity to one or two

organs[1]. These are referred to as target organs of toxicity for the substance. Two classes of target organ toxicity are defined Specific target organ toxicity - single exposure (STOT-SE) and Specific target organ toxicity - repeat exposure (STOT-RE)

- **STOT-SE (Specific Target Organ Toxicity - Single Exposure)**: specific, non-lethal target organ toxicity arising from a single exposure to a chemical (example of acute effect). Substances with a STOT-SE are classified into 3 categories: **Category 1** substances have produced significant toxicity in humans, or, on the basis of evidence from studies in experimental animals, can be presumed to have the potential to produce significant toxicity in humans following single exposure ; **Category 2** substances, on the basis of evidence from studies in experimental animals, can be presumed to have the potential to be harmful to human health following single exposure ; **Category 3** substances produce transient (short duration or temporary) target organ effects such as narcotic effects or respiratory tract irritation

- **STOT-RE (Specific Target Organ Toxicity - Repeat Exposure)**: specific target organ toxicity arising from repeated exposure to a substance or mixture (example of chronic effect). Substances with a STOT-RE are classified into 2 categories: **Category 1** substances have produced significant toxicity in humans, or, on the basis of evidence from studies in experimental animals, can be presumed to have the potential to produce significant toxicity in humans following repeated or prolonged exposure ; **Category 2** substances, on the basis of evidence from studies in experimental animals, can be presumed to have the potential to be harmful to human health following repeated or prolonged exposure

- **Neurotoxicity**: ability of inducing adverse effects on the nervous system, which can result for example in confusion, fatigue, irritability, or other behavioral changes. Source of information, see: http://scorecard.goodguide.com/health-effects/chemicals-2.tcl?short_hazard_name=neuro&all_p=t

- **Immunotoxicity**: ability of inducing adverse effects on the functioning of the immune system. Altered immune function may lead to the increased incidence or severity of infectious diseases or cancer, since the immune system's ability to respond adequately to invading agents is suppressed. Allergens, which are compounds that stimulate the immune system and can cause hypersensitivity reactions or allergies, are considered to be immunotoxicants. Source of information, see http://scorecard.goodguide.com/health-effects/chemicals-.tcl?short_hazard_name=immun&all_p=t

- **Endocrine disruptor**: exogenous substance or mixture that alters function(s) of the endocrine system and consequently causes adverse health effects in an intact organism, or its progeny, or (sub) populations ; a potential endocrine disruptor is an exogenous substance or mixture that possesses properties that might be expressed to lead to endocrine disruption in an intact organism, or its progeny, or (sub) populations (World Health organization (WHO) International Programme on Chemical Safety (IPCS) definition**,** see http://www.who.int/ceh/publications/endocrine/en/). See also EU priority list: http://ec.europa.eu/environment/chemicals/endocrine/

- **SVHCs (Substances of Very High Concern)**: substances deemed very hazardous with respect to human health and the environment and which come under scrutiny for authorization or restriction under REACH. Human health concerns includes substances classified as Carcinogens

[1] *Toxicology, the Basic Science of Poisons from* Casarett and Doull's

Cat 1 & 2, Mutatoxic and Reprotoxic Cat 1 & 2, and substances with can interfere with the hormone system (endocrine disruptors). Substances which are of high concern to the environment include PBTs, vPvBs. See: https://echa.europa.eu/candidate-list-table

- **Respiratory sensitization**: ability of inducing hypersensitivity of the airways following inhalation

- **Emerging substance**: substances that have been detected in the environment, but which are currently not included in routine monitoring programmes at EU level and whose fate, behavior and (eco)toxicological effects are not well understood[2]

Section 5: Exposure characteristics

- **E-PRTR (European Pollutant Release and Transfer Register)**: Europe-wide register providing key environmental data from industrial facilities in European Union Member States and in Iceland, Liechtenstein, Norway, Serbia and Switzerland. Contains data reported annually by more than 30,000 industrial facilities covering 65 economic activities across Europe. For each facility, information is provided concerning the amounts of pollutant releases to air, water and land as well as off-site transfers of waste and of pollutants in waste water from a list of 91 key pollutants including heavy metals, pesticides, greenhouse gases and dioxins. See http://prtr.ec.europa.eu/#/home

- **Multisource exposure**: exposure to the substance through various media (e.g. air, water, soil, food, consumer products)

- **PBTs (Persistent, Bioaccumulative and Toxic)**: substances defined as toxic, persisting in the environment and bioaccumulating in food chains and, thus, posing risks to human health and ecosystems. PBTs transfer rather easily among air, water, and land, and span boundaries of programs, geography, and generations. See https://echa.europa.eu/

- **vPvB (very Persistent and very Bioaccumulative) substances**: substances of very high concern, which are very persistent (very difficult to break down) and very bio-accumulative in living organisms. See https://echa.europa.eu/

- **Natural exposure:** non-anthropogenic release of the substance

- **Anthropogenic exposure**: release of the substance through human-made activities

- **Volume of production**: tonnage manufactured and/or imported per year to the European Economic Area (EEA), which is published (or registered) on ECHA database (data may be claimed confidential and may not be available). See https://echa.europa.eu/

- **ECHA (European Chemicals Agency):** EU agency which manages the technical, scientific and administrative aspects of the implementation of the EU regulation REACH. See https://echa.europa.eu/

- **Vulnerability**: defined in this context as the diminished capacity of an individual or group to cope with, resist and recover from the impact of a natural or man-made hazard, depending from physical, economic and social factors for example[3]

[2] See Norman website: http://www.norman-network.net/
[3] http://www.ifrc.org/en/what-we-do/disaster-management/about-disasters/what-is-a-disaster/what-is-vulnerability/

- **Exposure routes**: routes by which substances can enter the body, which in the case of environmental pollutants are dermal absorption, inhalation, ingestion (oral absorption) or transplacental transfer

- **Widespread use by professional workers**: uses carried out in the context of commercial activities and assumed to take place in most towns of a certain size, by multiple actors each at low scale e.g. local garage, small cleaning businesses. They are also considered end-uses. The further fate of the substance corresponds to the fate as described for uses at industrial sites[4]

- **Consumer use**: all end-uses of the substance as such or in a mixture carried out by consumers can be reported under this life cycle stage. Uses by consumers are also considered to take place in a widespread manner[3]

- **Biomonitoring data**: measurements of the levels of indicators of chemicals uptake (known as biomarkers) in biological matrices, as body fluids (e.g. blood, hair, saliva or urine) or tissues (e.g. hair, nails, fat, and bone)

Section 6: Regulatory status

- **Toxicity Reference Value (TRV)**: toxicological index used to qualify or quantify a risk to human health when compared with exposure. TRVs are established for a given critical effect, and are specific to a substance, a duration of exposure (acute, subchronic or chronic) and a route of exposure (oral, inhalation, etc.). Their derivation depends on available data on the substances' toxicological mechanisms of action and commonly accepted assumptions: a distinction is therefore made between "TRVs without a threshold dose" and "TRVs with a threshold dose"[5]. According to the (inter)national agencies derivating TRVs, TRVs with a threshold dose can be referred as:

Agency	Acronym	Name	Pathway
TRV in the general population			
ANSES	**VTR**	Valeur Toxicologique de Référence à seuil de dose	Oral & inhalation
	DJA	Dose Journalière Admissible	Oral
	DJT	Dose Journalière Tolérable	
	DHT	Dose Hebdomadaire Tolérable	
	DMT	Dose Mensuelle Tolérable	Oral & inhalation
ATSDR	**MRL**	Minimum Risk Level	Oral & inhalation
EFSA	**ADI**	Acceptable Daily Intake	Oral
	TDI	Tolerable Daily Intake	Oral
	TWI	Admissible Tolerable Weekly Intake	Oral
	TMI	Tolerable Monthly Intake	Oral
OEHHA	**REL**	Reference Exposure Levels	Oral & inhalation
RIVM	**MPR**	Maximum Permissible Risk level	Oral & inhalation

[4] https://echa.europa.eu/documents/10162/13632/information_requirements_r12_en.pdf
[5] Anses website: https://www.anses.fr/en/content/trvs-toxicity-reference-values

	ADI	Acceptable Daily Intake	Oral
	TCA	Tolerable Concentration in Air	Inhalation
	TDI	Tolerable Daily Intake	Oral
WHO	**TCA**	Tolerable Concentration in Air	Inhalation
	ADI	Acceptable Daily Intake	Oral
	TDI	Tolerable Daily Intake	Oral
	TWI	Admissible Tolerable Weekly Intake	Oral
Health Canada	**ADI**	Admissible Daily Intake	Oral
	TDI	Tolerable Daily Intake	Oral
	CA	Admissible Concentration in Air	Inhalation
US EPA	**RfD**	Reference Dose	Oral
	RfC	Reference Concentration	Inhalation
TRV in the workplace			
ACGIH	TLV-TWA	Threshold Limit Values - Time Weighted Average	
	TLV-STEL	Threshold Limit Values- Short Term Exposure Limit	
	TLV-C	Threshold Limit Value - Ceiling	
ANSES	VLEP-8h	Valeur Limite d'Exposition Professionnelle (8 heures)	
	VLCT-15 min	Valeur Limite Court Terme (15 minutes) (VLCT-15 min)	
	-	Valeur plafond	
Danemark	TWA-8h	Time Weighted Average-8h	
	STEL	Short TErm Limit	
DECOS	TWA-8h	Time Weighted Average-8h	
	STEL	Short TErm Limit	
DFG	MAK	Maximale Arbeitsplatzkonzentrationen	
NIOSH	REL–TWA	Recommended Exposure Level-Time Weighted Average	
	REL-ST	Recommended Exposure Level- Short-Term exposure limit	
	REL-C	Recommended Exposure Level – Ceiling	
OSHA	PEL-TWA	Permissible Exposure Level-Time Weighted Average	
	PEL-STEL	Permissible Exposure Level- Short-Term exposure limit	
SCOEL	TWA	Occupational Exposure Limit Time Weighted Average	
	STEL	Occupational Exposure Limit Short Term Exposure Limit	

According to the (inter)national agencies derivating TRVs, TRVs without a threshold dose can be referred as:

Agency	Acronym	Name	Pathway
ANSES	**VTR**	Valeur Toxicologique de Référence sans seuil de dose	Oral & inhalation
OEHHA	**-**	Oral Slope Factor	Oral

	-	Unit Risk Factor	Inhalation
WHO	**-**	Inhalation Unit Risk	Inhalation
	-	Oral Slope Factor	Oral
RIVM	**CR**	Excess lifetime cancer risk	Oral & inhalation
	MPR	Maximum Permissible Risk level	Oral & inhalation
Health Canada	**TD** $_{0,5}$	Tumorigenic Dose $_{0,5}$	Oral
	TC $_{0,5}$	Tumorigenic Concentration $_{0,5}$	Inhalation
US EPA	**IUR**	Inhalation Unit Risk	Inhalation
	OSF	Oral slope factor	Oral
	-	Drinking Water Unit Risk	Oral

- **Biomonitoring guidance values - *provisional definition***: *represents a certain concentration or range of concentrations of a chemical or its metabolite in a biological medium (blood, urine, or other medium) that is consistent with an existing health-based exposure guideline, or associated with exposures that are consistent with general population exposure guidance values. Different types of biomonitoring guidance values exist, as for example*:

Agency	Acronym	Name
Biological Guidance Values in the general population		
ANSES	**VBR**	Valeur Biologique de Référence
DFG	**BAR**	Biologische Arbeitsstoff-Referenzwerte
SCOEL	**BGV**	Biological Guidance Values
UBA	**HBM-I or -II**	Human biomonitoring value-I or -II
	BE	Biomonitoring Equivalent
	BAT	Biologische Arbeitsstoff-Toleranzwerte
Occupational Biological Guidance Values		
ANSES	**VLB**	Valeur Limite Biologique
SCOEL	**BLV**	health-based Biological Limit Value
ACGIH	**BEI**	Biological Exposure Indices
DFG	**BAT**	Biologischer Arbeitsstoff Toleranzwerte
	BLW	Biologischer Leit-Wert
	EKA	Expositionsäquivalente für Krebserzeugende Arbeitsstoffe
FIOH	**BAL**	Biological Action Level
HSL	**BMGV**	Biological Monitoring Guidance Value
SUVA	**VBT**	Valeur Biologique Tolérable

- **Potential for exposure prevention or reduction**: feasibility of exposure prevention or reduction, e.g. availability of substitutes or alternative industrial process (taking into accounts technical,

economic and social implications) from environmental sources (for the general population) and/or occupational settings (for workers)