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Taste & Odor compounds in drinking water: are they an actual concern for human health?

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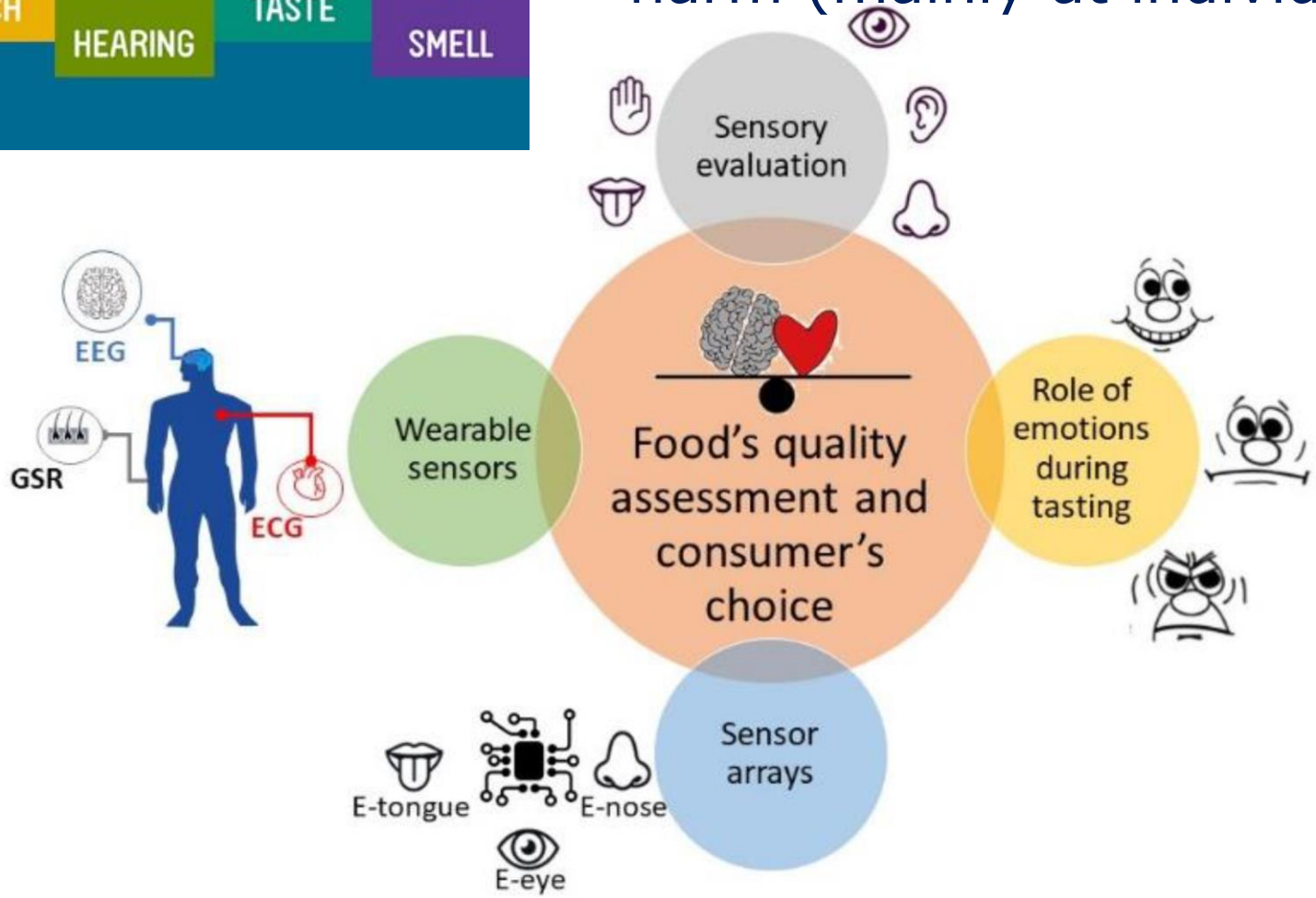
Humans primarily assess risk through their **5 senses**, relying on

to make **informed choices**, especially in selecting food and water to avoid potential harm (mainly at individual-subjective level)



Does this mean that what is not able to affect our sense is safe and /or that T&O compounds are all toxic?

The answer is definitely: NO

Serious chemical threats (of synthetic and natural origin) often go unnoticed, as they may lack color, taste and odor

T&O characteristics can help in limiting exposure

RISK = HAZARD x EXPOSURE

In the context of drinking water, volatile compounds responsible for unpleasant tastes and odors or colour is deemed unsuitable for consumption by human and animal due to its organoleptic properties, preventing exposure.

They are generally not considered a health risk through oral exposure: the concentrations required to induce adverse effects are considerably higher than their odor threshold concentrations (OTC).

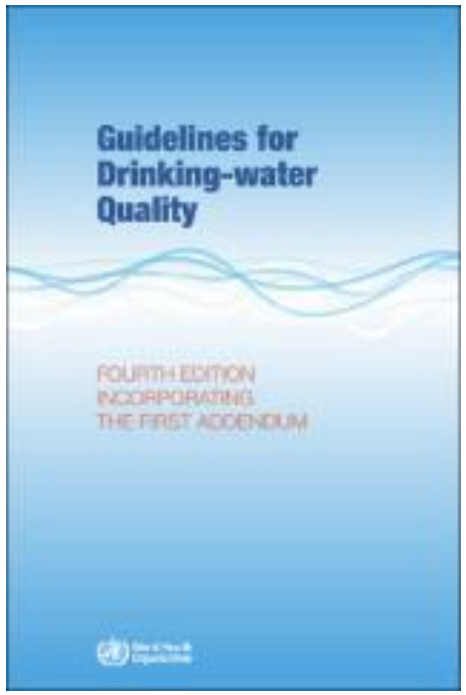
This reasoning is not always valid….

- ✓ The perception and intensity of taste or odor may not reliably indicate low compound concentrations, as the concentration-to-intensity relationship is not well understood
- ✓ Sensory detection of these compounds can vary among individuals and even within the same person over time (perception is very subjective)
- ✓ Interactions among odor-producing substances can lead to a significant increase in odor thresholds
- ✓ The perception of unpleasantness is often very different for human and animals (e.g. the 'fatal attraction' of animals for water contaminated by cyanobacteria)

Maintaining a substantial margin (e.g., >100) between OTC and the Guidance Value (GV) is essential

What is and how is a GV derived?

World Health Organization



WHO produces **international norms on water quality and human health in the form of guidelines** that are used as the basis for regulation and standard setting world-wide for water safety in support of public health.

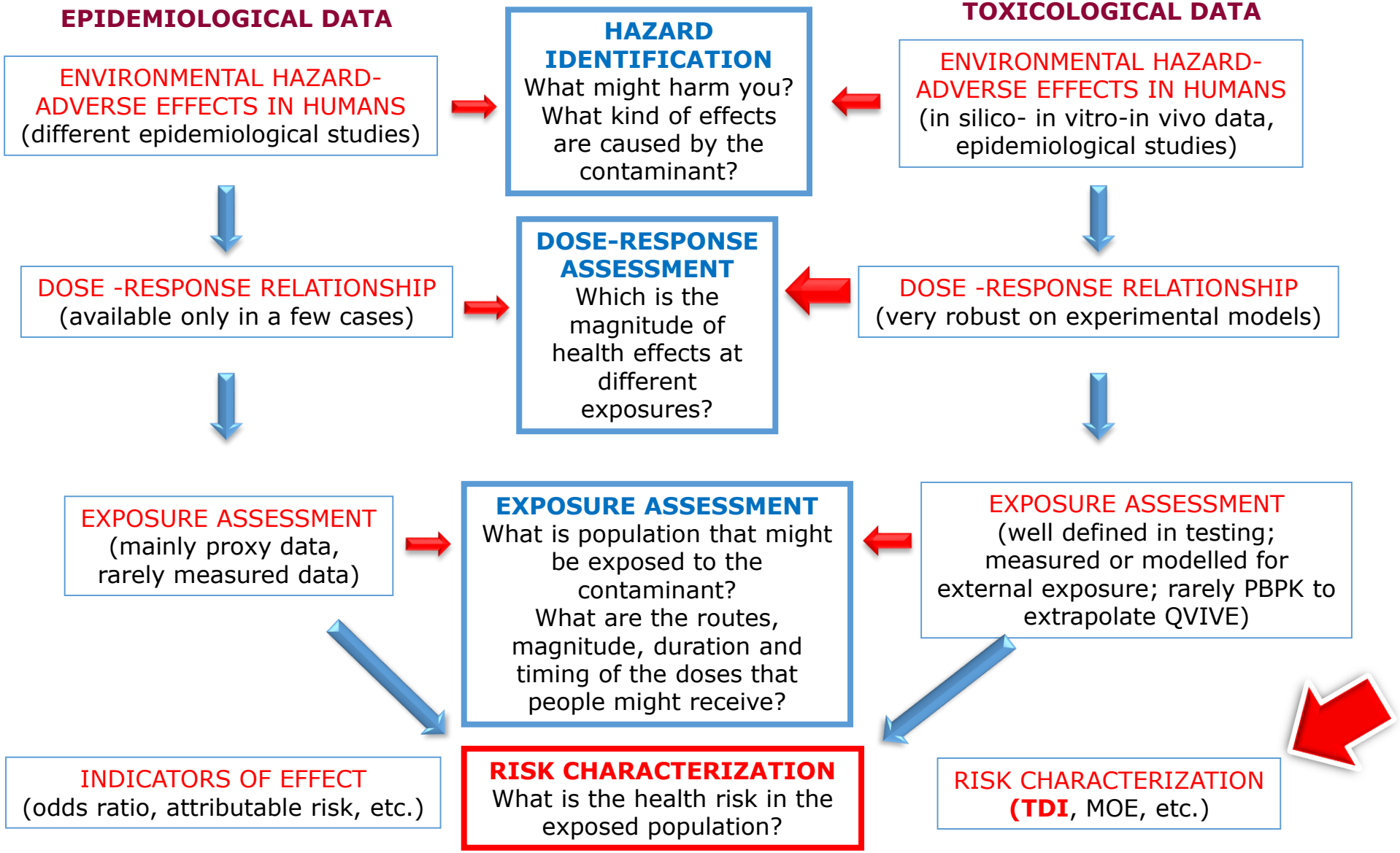
The Guidelines for drinking-water quality (GDWQ) promote the **protection of public health**, recommending preventive risk management approaches covering catchment to consumer **(Water Safety Plans)**.

The GDWQ include an **assessment of the health risk** presented by the various microbial, **chemical**, radiological and physical constituents that may be present in drinking-water.

The GDWQ derive numerical "guidelines values" (GV) for constituents of water or contaminats, describing **the approaches used in deriving** GV and explain how the GDWQ are intended to be used.

The GV corresponds to the concentration of a chemical that can be present in drinking water without causing any appreciable adverse effect in an adult (of 60 kg bw) consuming daily 2L of drinking water over the entire lifespan.

The 4 STEPs in RISK ASSESSMENT



Please see the material available on the WATERTOP website for details (Training school in RA – Rome October 2023)

Guidance Values (GV) Derivation

GV= maximum concentration acceptable in each single source of exposure (i.e.: drinking water)

$$GV = \frac{TDI \times body\ weight \times All.F}{daily\ intake}$$

TDI= Tolerable Daily Intake = expressed as mg/kg bw per day= the daily dose below which it is assumed that adverse effects are unlikely to occur in humans exposed to the substance for the entire life span (estimated 70 years long).

All.F= allocation factor= % of TDI attributable to every single source of exposure (taken the sum of them as 100%)

Daily intake =2L

Body weight =60 kg

The recommended drinking water GVs are derived to protect human health with respect to **lifetime consumption**. They are generally lower than those considered 'safe' for short-term exposure, as it could be for many T&O compounds. GVs represent a conservative approach to estimate possible risk associated to the presence of T&O.

The WHO GDWQ report a list of T&O compounds in drinking water with OTC at concentrations well below those which can cause adverse health effects, therefore for most of them no GVs have been derived.

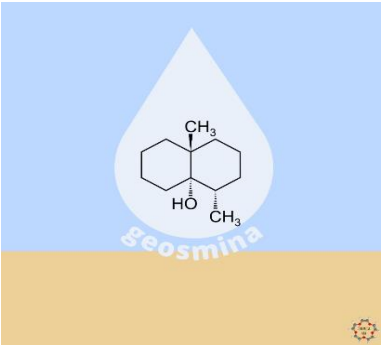
β-ionone : estimated OTC is 7 ng/L
The acceptable daily intake is about 0.1 mg/kg bw (GV around 0.6 mg/L)
The OCT is more than two orders of magnitude lower than GV : T&O feature prevents exposure via drinking water and β-ionone in DW does not represent a health risk.

Toluene : OTC in water is in the range 24-170 µg/L
The health-based GV of 700 µg/L.
It is unlikely for the population to drink toluene-contaminated water at concentrations above the GV. However, since the ratio 700/170 is only =4, the reliability of the detection methods for OTC (e.g. subjective judgment of assessors) can be relevant and the risk cannot be fully excluded

Xylene : the OTC range from 0.02 to 1.8 mg/L
The health-based GV is 0.5 mg/L for xylene, same order of magnitude of the OTC
The odor may not constitute a warning measure for exposure and could be potentially associated with a health risk for consumers, since consumers can easily drink water containing xylene concentrations higher than the GV without complaining

The toxicological profiles of most T&O compounds remain inadequately characterized, hindering proper risk assessment.

GEO:



- ✓ The OTC of GEO has been set between 1.3–1.0 ng/L
- ✓ The current consensus is that GEO is nontoxic to humans via DW at environmentally relevant concentrations (in the high nanomolar up to the low micromolar range).
- ✓ These conclusions mainly derive from work showing that the concentrations at which GEO inuces adverse effects in aquatic organisms are three orders of magnitude higher than the human OTC
- ✓ The only consistent result is the lack of genotoxic potential. When cells of mammalian origin were used in vitro their relevance was limited by the relevance of the model or by flawed study design.
- ✓ Overall results appear to indicate a low potential for inducing significant health effects in vivo, but the need for quality toxicological data is highlighted

When available toxicity data are lacking (other T&O or water purification by-products) the use of in silico approaches becomes the only available choice

Read Across : If information on structurally similar chemicals are available it is possible to apply the read across principle

The toxicological profile of chemical A is known (source chemical), scant info available for chemical B

If you can support with **in silico analysis** (e.g. SAR Structure activity relationship) the structural similarity, or with '**bridging studies**' (both in vitro and in vivo) the similarity of A and B toxicological profiles, the read across principle can be applied.

ECHA: Pratical Guidance 6
http://echa.europa.eu/documents/10162/13655/pg_report_readacross_it.pdf
http://echa.europa.eu/support/grouping-of-substances-and-read-across

OECD: GUIDANCE ON GROUPING OF CHEMICALS, SECOND EDITION Series on Testing & Assessment No. 194 (2014)
http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2014)4&doclanguage=en

EFSA : Opinion on grouping for combined risk assessment (2021)

QSAR

The quantitative structure-activity relationship (QSAR) is a mathematical model that quantitatively expresses the biological activity of a molecule as a function of certain chemical-physical or structural characteristics of the molecule (structure, polarity, bulk, orbitals , etc.)

Not all the methods are suitable for any chemical or group of chemicals. The applicability domain (AD) is 'a theoretical region in physicochemical space' (the response and chemical structure space) for which a QSAR model should make predictions with a given reliability.
The AD determines types of molecules and toxicity endpoints to which the model can be applied.

Even within the AD the prediction of a model is good only if the quality of the input data is good.
The GIGO rule is always valid !

Garbage In → Garbage Out

Threshold of Toxicological Concern (TTC)

In case you have to evaluate the safety of chemicals for which information are not available

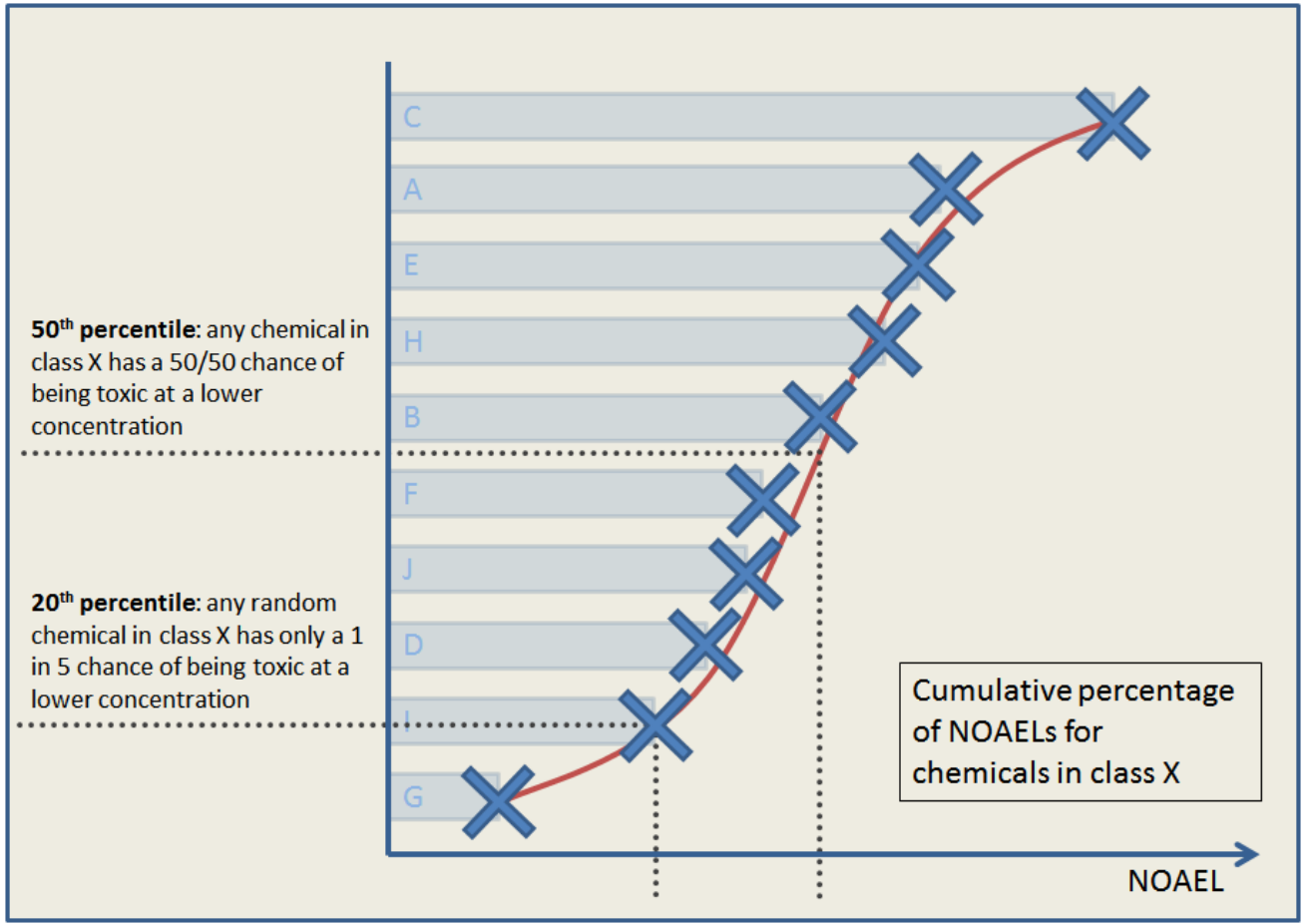
- *The TTC approach is a **science-based pragmatic tool for screening and prioritizing chemicals** for their safety assessment when hazard data are lacking or incomplete and human exposure can be estimated.*
- It has been developed to qualitatively assess the risk of low-level substances in the diet. It can be used for an initial assessment of a substance to determine whether a comprehensive risk assessment is required or to **prioritise chemicals** that require more data over those that can be presumed to present no appreciable human health risk.
- If the chemical structure of a substance is known, health risk can be evaluated on the basis of **generic human thresholds of exposure – "TTC values"**. TTC values have been established for substances of similar chemical structure and likelihood of toxicity**, based on extensive published toxicological data**.

Threshold of Toxicological Concern (TTC)

There are three broad categories of low, moderate or high toxicity defined as substances in **Cramer class 1, 2 and 3** respectively, based on the chemical structure and various alerts (see specific lessons on the use of the OECD tool box)

The TTC values were determined by statistically analyzing substantial toxicological databases and other available toxicity data (NOEL, LOAEL, etc).

TTC uses distributions of NOAELs for substances. The 5th percentile value is divided by an uncertainty factor (100) to give a TTC value.



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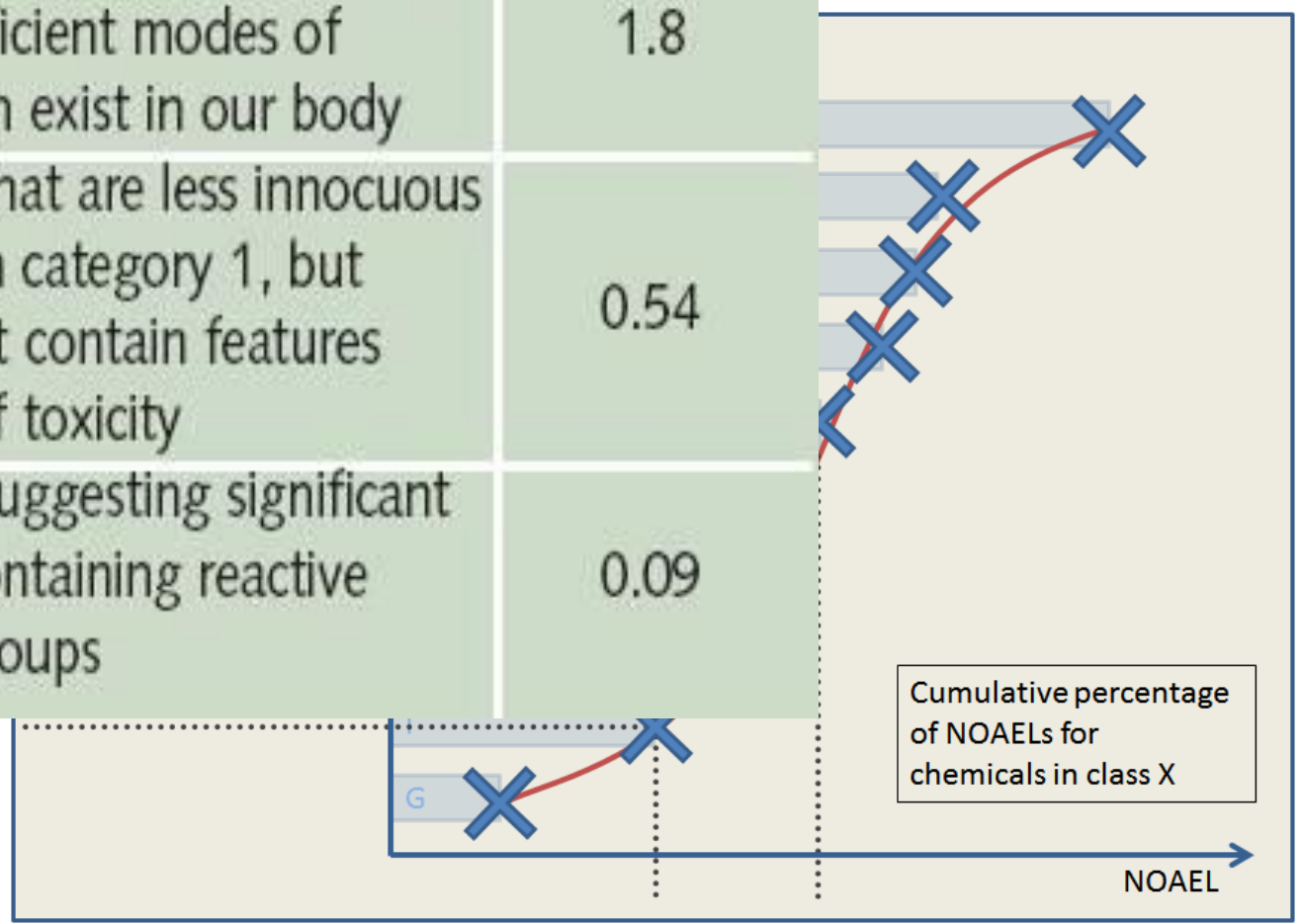
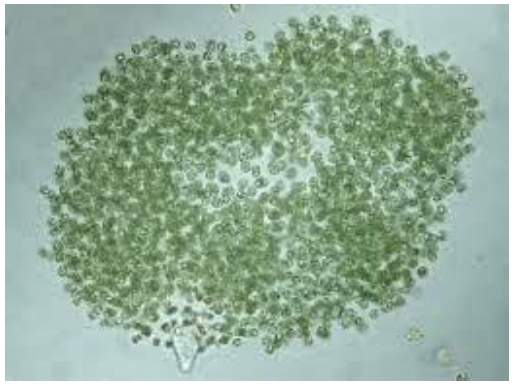
The TTC va[illegible]oxicological databases [illegible]

TTC uses [illegible] of NOAE[illegible] The 5th [illegible] divided [illegible] factor (1[illegible] value.

Category	Description	TTC mg/ person/day
1. Low toxicity	Substances with simple structures for which efficient modes of detoxification exist in our body	1.8
2. Moderate toxicity	Substances that are less innocuous than those in category 1, but which do not contain features suggestive of toxicity	0.54
3. High toxicity	Substances suggesting significant toxicity or containing reactive functional groups	0.09



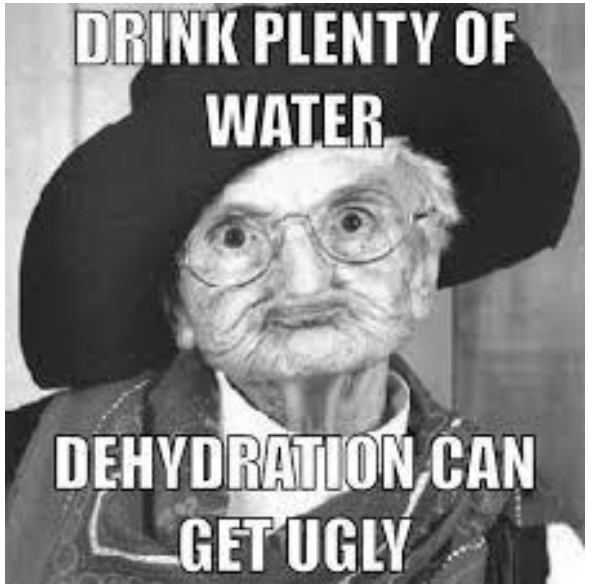


- **β–cyclocitral (or isocyclocitral)** has been identified as produced exclusively by *Microcystis*.
- By consulting ECHA public information no harmonized classification was found, only an oral acute toxicity study is cited.

The **evaluation of β-cyclocitral toxicity with the TTC approach**

- β–cyclocitral belongs to **Cramer Class I** (characterized by low toxicity) and therefore, levels below the threshold of **1800 µg/person per day** are expected not to induce any relevant health effect in an adult of 60 Kg bw.
- About **12 µg/L** can be present in dissolved form in the water after cell rupture (e.g., in senescent blooms), but peak values as high as 400–2000 µg/L were reported.
- Considering the difficulties in removing T&O compounds from the water via traditional water treatment processes, the consumption of 2 L of drinking water per day is expected to be lower than the TTC for β-cyclocitral after oral exposure although a potential risk can arise only during sporadic events.

THANKS!


DRINK PLENTY OF WATER
DEHYDRATION CAN GET UGLY


THE BEST WAY TO SELL ME WATER
NON-ALCOHOLIC VODKA