




# FoodSafety4EU

MULTI-STAKEHOLDER PLATFORM  
FOR FOOD SAFETY IN EUROPE

## Manual for use of the risk assessment toolkit

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## Foreword

Dear user

Thank you for your interest in using the risk assessment toolkit designed by the FoodSafety4EU consortium. Its use is intended for (food) scientists, students and other stakeholders who are interested to learn more about risk assessment. The toolkit comprises two separate excel documents: one standard format for chemical data collection and one calculation spreadsheet for risk assessment. Within this document, you will discover comprehensive instructions outlining the step-by-step procedure for conducting a chemical risk assessment. It is important to note that the toolkit has been specifically designed to provide a rapid estimation of the risk associated with a chemical food contaminant, employing straightforward deterministic calculations. However, it is essential to recognize that the toolkit does not consider uncertainties and data distributions and, as a result, may potentially overestimate the risk. Moreover, risk assessment encompasses complex steps that vary depending on the availability of data. This toolkit will not guide you to perform a chemical risk assessment from scratch, but helps in following the steps if a considerable amount of information, *eg.* reference values and toxicological information, is already available. For extensive risk assessment, we refer to guidance documents of for instance the World Health Organization (WHO) or the European Food Safety Authority (EFSA), as referred in the last chapter of this document. Nonetheless, the toolkit offers a valuable overview of the various steps involved in the risk assessment process, enabling you to comprehend the underlying calculations.

To facilitate your experience, the risk assessment process will be elucidated using T2 and HT-2 toxins as an illustrative example. These particular compounds are classified as mycotoxins and fall under the category of chemical food contaminants.

We hope that the toolkit will prove to be a valuable resource in risk assessment journey.

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# INDEX OF CONTENTS

1	INTRODUCTION.....	5
1.1	What is risk assessment? .....	5
1.2	The toolkit in brief.....	6
2	Risk assessment: step by step guidance for use of the toolkit .....	6
2.1	Hazard identification .....	6
2.2	Hazard characterization .....	7
2.3	Exposure assessment .....	8
2.4	Risk characterization .....	11
3	Concluding remarks .....	13

# 1 INTRODUCTION

## 1.1 What is risk assessment?

Risk assessment of chemical food contaminants is a systematic process that evaluates the potential hazards associated with food consumption and quantifies the level of risk to human health. The risk assessment process aims to provide a scientific basis for decision-making and the implementation of effective control measures.

The risk assessment process typically consists of four key steps: hazard identification, hazard characterization, exposure assessment, and risk characterization. Let's explore each step in more detail:

### 1) Hazard Identification

The first step in the risk assessment process is to identify potential hazards that may pose a threat to human health. In general, hazards can arise from various sources, such as biological (e.g., pathogens), chemical (e.g., contaminants), or physical (e.g., foreign objects) factors. For this toolkit, we only focus on chemical hazards. This step involves gathering relevant data, conducting literature reviews, and consulting experts to identify known hazards and their associated adverse health effects.

### 2) Hazard Characterization

Once hazards are identified, the next step is to characterize their nature and the potential harm they can cause. This involves evaluating the available scientific evidence, including toxicity studies, epidemiological data, and dose-response relationships, to determine the severity and likelihood of adverse health effects resulting from exposure to the hazard. Hazard characterization helps to establish the basis for setting health-based guidance values or reference points.

### 3) Exposure Assessment

Exposure assessment focuses on determining the extent to which individuals or populations come into contact with the hazard and estimating the levels of exposure. It involves evaluating various factors, including consumption patterns, food processing practices, contamination levels, and population demographics. Exposure assessment utilizes data from surveys, food consumption databases, monitoring programs, and other relevant sources to quantify the potential intake of the hazardous substance by the population.

### 4) Risk Characterization

The final step is to integrate the information obtained from hazard identification, hazard characterization, and exposure assessment to estimate the level of risk posed by the hazard. Risk characterization involves the quantitative estimation of the likelihood and magnitude of adverse health effects associated with specific levels of exposure. This step usually also considers uncertainty and variability in the data and may involve the use of modeling techniques or statistical analyses to generate risk estimates. However, for education purposes and simplicity, we will not use modeling techniques in this toolkit. The output of risk characterization provides a measure of the potential harm to human health and helps inform risk management decisions.

It is important to note that risk assessment is not a one-time process but rather an ongoing and iterative endeavor. As new scientific evidence emerges, the assessment should be periodically reviewed and updated to ensure its accuracy and relevance. Risk communication also plays a critical role throughout the process, as the findings and conclusions need to be effectively communicated to relevant stakeholders, including policymakers, industry professionals, and consumers.

The results of a chemical food risk assessment serve as a basis for risk management decisions, which involve implementing measures to control and mitigate the identified hazards. Risk management strategies may include setting regulatory limits, establishing good agricultural and manufacturing practices, implementing monitoring programs, conducting inspections, and providing consumer education. Risk assessment and risk management work together to ensure that the food supply is safe and that potential risks are effectively managed to protect public health.

## 1.2 The toolkit in brief

The risk assessment toolkit consists of two excel files: one data collection sheet that is optional to use for gathering new occurrence data, and one excel file that is helpful to execute a risk assessment after collection of relevant data (either by own data generation or collection of existing data).

The data collection sheet is designed to rapidly gather data on a limited number of chemical food contaminants in limited matrices. It is based on the standard sample description format (SSD2 format) established by the European Food Safety Authority (EFSA), but allows for simplification when data is used for rapid risk assessment. The reader is however encouraged to submit any analytical data to EFSA, using their simplified SSD2 excel template, which is also accompanied by instructions on Zenodo: <https://zenodo.org/record/4697332>.

The risk assessment tool is designed to rapidly assess risks of chemical food contaminants, using simple descriptive statistics. The user is required to insert data on existing toxicological reference values, contamination data and consumption data. Using this input, the tool will calculate all necessary values to assess the risks related to the food contaminant.

# 2 Risk assessment: step by step guidance for use of the toolkit

## 2.1 Hazard identification

Food chemical hazard identification is a crucial step in assessing the potential health risks associated with a specific food contaminant. The goal is to gather and analyze all available information on the substance's toxicity and its impact on the human body. This process helps to answer two key questions: 1) What are the potential health risks posed by the substance to humans? and 2) Under what conditions can these risks be observed?

To identify hazards, it is important to review and analyze various types of data, including studies conducted on humans, animals, and in laboratory settings. Additionally, examining the structure and activity of the substance is essential. By doing so, you can determine the specific toxic effects and identify the organs or tissues that may be affected.

Hazard identification for your specific compound of interest may have already been conducted, possibly by organizations such as EFSA. To enhance your understanding of the risk assessment process, it is highly recommended to briefly review previous work and highlight the main findings within the excel tool (**cell B2 of the risk assessment sheet**). This will provide valuable context for conducting a comprehensive risk assessment using the toolkit.

### Example

T2 and HT-2 toxin are type A trichothecenes produced under cool and moist conditions before harvest. Cereal grains, particularly oats, and their derivatives are the primary sources where T2 and HT-2 toxin are

predominantly found (EFSA, 2017). EFSA performed a hazard identification in 2011. Briefly, T2 induces ribotoxic and oxidative stress and inhibits DNA, RNA and protein synthesis. T2 has been shown to cause apoptosis and lipid peroxidation, affecting cell membrane integrity. Recent investigations also suggest that T2/HT-2 induces anorexia/emesis via alteration of pro-inflammatory cytokines and satiety hormones (EFSA 2011). The available information on the toxicokinetics of T-2 and HT-2 toxins is incomplete. T-2 toxin is rapidly metabolised to a large number of products, HT-2 toxin being a major metabolite. The metabolic pathways include hydrolysis, hydroxylation, de-epoxidation, glucuronidation and acetylation. Distribution and excretion of T-2 toxin and its metabolites are rapid. There are no significant data available on the toxicity of most metabolites. De-epoxidation is believed to be a detoxification process.

→ The findings are inserted in the risk assessment tool in the section of hazard identification (Figure 1).

1. HAZARD IDENTIFICATION	
Briefly describe the potential hazards to humans that the presence of a substance in food may pose	T2 induces ribotoxic and oxidative stress and inhibits DNA, RNA and protein synthesis. T2 has been shown to cause apoptosis and lipid peroxidation, affecting cell membrane integrity. Recent investigations also suggest that T2/HT-2 induces anorexia/emesis via alteration of pro-inflammatory cytokines and satiety hormones (EFSA 2011). The available information on the toxicokinetic of T-2 and HT-2 toxins is incomplete. T-2 toxin is rapidly metabolised to a large number of products, HT-2 toxin being a major metabolite. The metabolic pathways include hydrolysis, hydroxylation, de-epoxidation, glucuronidation and acetylation. Distribution and excretion of T-2 toxin and its metabolites are rapid. There are no significant data available on the toxicity of most metabolites. De-epoxidation is believed to be a detoxification process.

Figure 1: Printscreen of the risk assessment tool in Excel, where information on hazard identification is inserted in the corresponding cell of the hazard identification section.

## 2.2 Hazard characterization

Hazard characterization involves understanding the relationship between the dose or exposure to a chemical and the occurrence of adverse health effects. The focus is on determining the critical effect in the most sensitive species, which refers to the first adverse effect observed as the dose or exposure increases.

Similar to hazard identification, chances are high that a (preliminary) hazard characterization has already been performed and that you can find information in literature to proceed with the risk assessment.

The first step is to establish whether the compound of interest is a genotoxic carcinogen. You can find this information in the OpenFoodTox database, specifically in the file "Genotoxicity\_KJ" on the Zenodo platform: <https://zenodo.org/record/3693783>. Identifying genotoxic/carcinogenic compounds is important because their risk characterization is more stringent compared to other chemicals, as they have the potential to cause damage without a threshold. It is known that the majority of chemical carcinogens are genotoxic.

### Genotoxic carcinogens

If your compound is identified as genotoxic and carcinogenic, you will need to find a corresponding reference point, typically the lowest limit of the confidence interval of the benchmark dose (BMDL<sub>10</sub>). This can be found in the file "ReferencePoints\_KJ" on the Zenodo platform: <https://zenodo.org/record/3693783>. In case a reference point cannot be found, you can use the standard threshold of toxicological concern (TTC) of 0.0025 µg/kg bw/day. Fill in the appropriate value in the risk assessment tool's corresponding **cell B5 of the risk assessment sheet**. If you have no value, put nothing in the cell.

### Non-genotoxic compounds

For non-genotoxic compounds, health-based guidance values (HBGVs) are commonly used in further calculations. These HBGVs can include acute reference doses (ARfD) for estimating the risk after acute exposure. The ARfD is the estimated intake of a chemical substance in food, expressed on a body weight basis, that can be ingested over a short period of time, usually during one meal or one day, without posing a health risk. For chronic exposure, other established HBGVs such as tolerable daily intake (TDI), acceptable daily intake (ADI), or tolerable weekly intake (TWI) can be used. You can find the AfRD and other HBGVs in the file "ReferenceValues\_KJ" on the Zenodo platform: <https://zenodo.org/record/3693783>. If no reference value is available, you can use a reference point such as the no observed adverse effect level (NOAEL) or

BMDL<sub>10</sub>, but with additional safety margins. In this toolkit however, for simplicity, it is recommended to estimate the TTC based on the Cramer classification if you cannot find a HBGV. The Cramer classification categorizes organic chemicals into three classes (I - low, II - intermediate, and III - high) based on their probability of low, moderate, or high toxicity. You can easily determine the Cramer Class using ToxTree by inserting the CAS number of the compound of interest in the upper right corner: <https://toxtree.sourceforge.net/predict/>. For compounds classified in Class I, use a TTC of 30 µg/kg bw/day; for compounds classified in Class II-III, use a TTC of 1.5 µg/kg. Fill in the appropriate values in the risk assessment tool's corresponding cells (**B10** for acute and **B14** for chronic of the risk assessment sheet). If you have no value, put nothing in the cell.

## Example

T2 and HT-2 are currently characterized as not genotoxic and carcinogenic. The EFSA Panel on Contaminants in the Food Chain (CONTAM) established a group TDI for T2 and HT-2 of 0.02 µg/kg body weight (bw) per day based on an *in vivo* subchronic toxicity study in rats that confirmed that immune- and haematotoxicity are the critical effects of T2 and using a reduction in total leucocyte count as the critical endpoint. An ARfD of 0.3 µg for T2 and HT2/kg bw was established based on acute emetic events in mink.

→ The findings are inserted in the risk assessment tool in the section of hazard characterisation in cell B10 and B14. (Figure 2)

2. HAZARD CHARACTERISATION			
* Genotoxic carcinogen?	RP in µg/kg bw/day	Type	References
Find genotoxicity evaluation in File <b>Genotoxicity_KJ</b> and specify <b>reference point (RP)</b> , from File <b>ReferencePoints_KJ</b> on the <b>OpenFoodTox database</b> (NOAEL, BMDL <sub>10</sub> -): <a href="https://zenodo.org/record/3693783">https://zenodo.org/record/3693783</a> If no RP: Use TTC of 0.0025 µg/kg bw/day		BMDL <sub>10</sub>	
* NOT genotoxic?			
ACUTE	ARfD in µg/kg bw/day		
Specify the acute reference dose (ARfD) from File <b>ReferenceValues_KJ</b> on <b>OpenFoodTox database</b> <a href="https://zenodo.org/record/3693783">https://zenodo.org/record/3693783</a>	0,3	ARfD	EFSA (2017). Appropriateness to set a group health based guidance value for T2 and HT2 toxin and its modified forms. EFSA Journal 15(1):4655).
CHRONIC	HGBV/TTC in µg/kg bw/day		
Specify health-based guidance value (HBGV) from File <b>ReferenceValues_KJ</b> on <b>OpenFoodTox database</b> (TTC, TDI, ADI, TWI...): <a href="https://zenodo.org/record/3693783">https://zenodo.org/record/3693783</a> If no HBGV: Specify Cramer Class using <b>Toxtree</b> . Class I: use TTC of 30 µg/kg bw/day; Class II-III: use TTC of 1,5 µg/kg <a href="https://apps.ideaconsult.net/data/ui/toxtree">https://apps.ideaconsult.net/data/ui/toxtree</a>	0,02	Group TDI	EFSA (2017). Appropriateness to set a group health based guidance value for T2 and HT2 toxin and its modified forms. EFSA Journal 15(1):4655).

Figure 2: Printscreen of the risk assessment tool in excel, where ArfD and HBGV are inserted in the corresponding cells of the hazard characterization section.

## 2.3 Exposure assessment

Exposure assessment involves quantitatively evaluating the potential intake of a chemical contaminant through food and other relevant sources of exposure. For simplicity, we will only focus on exposure after oral intake of food. The measurement of exposure is typically expressed as intake in kg per kilogram of body weight per day (kg/kg bw/day).

To conduct the exposure assessment, two types of data need to be collected: 1) occurrence data, which refers to the presence of the chemical contaminant in a specific food of interest, and 2) consumption data, which pertains to the amount of that specific food consumed by the population. Statistical parameters such as the mean and 95th percentile can then be calculated to obtain simple point estimates. By multiplying the estimates of contamination and consumption, the exposure can be determined, either acute or chronic.

For example, let's consider a situation where the mean contamination of a chemical in whole wheat bread is 1 mg/kg, and the average consumption of that bread is approximately 100 grams (0.1 kg) per day. In this case, an adult weighing 70 kg would be exposed to  $1 \text{ mg/kg} \times 0.1 \text{ kg per day} / 70 \text{ kg} = 0.0014 \text{ mg/kg bw/day}$ , assuming average consumption. It is important to note that other calculations can be performed using, for



instance, the 95th percentile to account for higher contamination and consumption scenarios. Since some bread samples may have higher contamination levels, and there are individuals in the population who consume more than the average amount of bread, the exposure levels will also be higher. Therefore, it is necessary to calculate different scenarios to estimate the risks associated with varying levels of exposure.

Furthermore, it is crucial to recognize that contamination levels in food can vary significantly between regions and batches. The absence of detecting the chemical contaminant of interest in a particular food does not imply its absence altogether. There is a possibility that the analytical methods used were not sensitive enough to detect it. Strategies have been proposed to address these situations, considering the presence of so-called non-detects in calculations and accounting for the potential low concentration of the contaminant. It is therefore important to organize the data into different scenarios. When dealing with contamination data, this involves creating a lower bound scenario, where non-detects are assumed to be zero, and an upper bound scenario, where non-detects are replaced with the limit of quantification (LOQ) of the analytical method used.

#### *Contamination data collection*

If you are planning to gather data of a chemical in certain foods first, you can use the FoodSafety4EU data collection format prepared in Excel. This data format helps to gather all relevant data about a chemical, and follows the standard sample description format of EFSA (SSD2). However, it is less detailed and is convenient to use when you want to collect data for a limited set of chemical contaminants and food products intended for your own risk assessment. Note that it is very important to get information on the analytical technique used, as you will need the LOQ for further calculations.

There is a separate sheet in the risk assessment toolkit called "Contamination data" where you can extract the necessary data for risk assessment from the data format (Sheet 3). In column **B**, you can insert all the contamination data belonging to a specific food sample. Make sure that the non-detects are included as '< LOQ'. In column **C**, you can state the LOQ of the analytical method per sample. In column **D** and **E**, you have to create two scenarios, where the < LOQ values are 0 (lower bound scenario, column **D**) and the LOQ value (upper bound scenario, column **E**), respectively. Finally, the tool will calculate the mean contamination levels for the lower and upper bound scenario, in column **F** and **G**, respectively. Note that the tool will only do calculations with the mean values. However, feel free to make extra calculations for other point estimates, eg. 95<sup>th</sup> percentiles.

#### *Consumption data collection*

To calculate exposure to a specific contaminant in a specific food product, you will need to collect data on the consumption of that food product. You can either do this by performing dietary surveys in the population of interest, or by consulting the database of EFSA with consumption data gathered in EU countries. To find this, go to <https://www.efsa.europa.eu/en/data-report/food-consumption-data>.

To register consumption of a certain food product, EFSA uses the FoodEx2 classification system, which consists of descriptions of a large number of individual food items aggregated into food groups and broader food categories in a hierarchical parent-child relationship. In the food consumption database, the consumption of these food categories is organised for different populations. You can go broad (Hierarchy L1-L3) or more specific (Hierarchy L4-L7). For more information on the food classification system of EFSA, consult <https://www.efsa.europa.eu/en/data/data-standardisation>.

When estimating the amount of a chemical residue in a specific food item consumed by people, it may be more appropriate to use food consumption data only from those individuals or days when the particular food was actually reported to be consumed ("consumers only" or "consuming days only"). This approach becomes crucial when dealing with foods that are rarely consumed since using statistics from the entire population or

all survey days could dilute the exposure significantly. However, it is important to note that relying solely on consumer-only data can lead to an overestimation of the long-term intake. This is because survey periods have time limitations, and individuals who did not report consuming a specific type of food within that period are not necessarily non-consumers of that food in the broader context. Therefore, while "consumers only" data is useful for specific calculations, a comprehensive understanding of dietary exposure requires considering broader factors and potential variations in consumption habits over time. Based on your own or expert interpretation, decide if you want to select "consuming days only" or "all consuming days" for acute exposure, and "consumers only" or "all subjects" for chronic exposure. Assessment of acute exposure to a single food commodity is typically calculated on consuming days only, since adverse effects are associated with short term exposure. Chronic exposure to a single food commodity is also typically calculated for consumers only, however, at a higher aggregation level (L1-3), the use of total population statistics may be preferred. Finally, you can also focus on specific age groups.

There is a separate sheet in the risk assessment toolkit to insert the consumption data of interest (sheet 4). There is a distinction between acute (columns **A** and **B**) and chronic consumers (columns **D** and **E**). Furthermore, two scenarios can be calculated for acute and chronic consumers: one for average consumers (column **A** for acute, **D** for chronic) and one for high consumers (column **B** for acute, **E** for chronic). Finally, different age classes can be included going from infants (0-11 months) to very elderly (older than 75). It will depend on the availability of data if a risk assessment for different age categories can be performed. If you have no value, put nothing in the cell.

### Example

In this example, we will calculate the exposure to the sum of T2 and HT-2 after consumption of oat bran by the Belgian population.

#### Contamination data

Contamination data of oats were retrieved from official controls in Belgium. In total, 126 sample results were received, of which 38 for oat bran specifically. Only two samples contained toxins in a concentration above the LOQ. The LOQ's ranged between 5 and 10 µg/kg. The results were pasted in column **B** of the "Contamination data" sheet, while the corresponding LOQ values were pasted in column **C**. Next, the lower and upper bound scenarios were created by replacing the LOQ by 0 and LOQ value, respectively. Finally, the tool calculated means for both scenarios in cell **F2** and **G2**, being 0.55 (lower bound) and 7.79 (upper bound) µg/kg, respectively. These values automatically appear in cell **B21** and **C21** of the risk assessment tool in sheet 2 (Figure 3).

3. EXPOSURE ASSESSMENT		CONTAMINATION DATA			
LB mean in µg/kg	UB mean in µg/kg				
0,55	7,786842105				

Figure 3: Printscreens of the risk assessment tool in Excel, where the mean contamination values of the lower and upper bound scenarios appear in the corresponding cells of the exposure assessment section.

#### Consumption data

Consulting the EFSA food consumption data base, statistical descriptors for oat bran were searched for Belgium, for all age categories. Oat bran was found to be classified in L4 as follows: Grain and grain-based products (L1) → Cereal grains and similar and primary derivatives thereof (L2) → Cereal bran (L3) → Oat bran (L4). The most recent data (i.e. from the Belgian food consumption survey of 2014) were used only. There were only results available for 'other children', 'adolescents' and 'adults'. The corresponding consumption

data were inserted in the 'Consumption data' sheet. The same consumption data automatically appear in the risk assessment tool sheet at sheet 2, between rows 25 and 31 (Figure 4)

	ACUTE CONSUMPTION DATA		CHRONIC CONSUMPTION DATA	
	Average consumers in kg/kg bw/day	High consumers in kg/kg bw/day (95th percentile)	Average consumers in kg/kg bw/day	High consumers in kg/kg bw/day (95th percentile)
24				
25				
26				
27	0,0019	0,00397	0,00119	0,0028
28	0,00073	0,00158	0,00039	0,00082
29	0,00063	0,00132	0,00042	0,00102
30				
31				

Figure 4: Printscreens of the risk assessment tool in Excel, where the mean and P95 consumption values of oat bran (acute and chronic) automatically appear in the corresponding cells of the exposure assessment section.

### Exposure assessment

Based on the input on the sheets "Contamination data" and "Consumption data", the tool can calculate all acute and chronic exposure values for different age categories, average and high consumers, and lower and upper bound scenarios. The results are visible between rows 36 and 42 of the risk assessment tool sheet (Figure 5).

	ACUTE EXPOSURE = CONTAMINATION X ACUTE CONSUMPTION				CHRONIC EXPOSURE = CONTAMINATION X CHRONIC CONSUMPTION			
	LB MEAN CONCENTRATION		UB mean CONCENTRATION		LB MEAN CONCENTRATION		UB mean CONCENTRATION	
	Average consumers (µg/kg bw/day)	High consumers (µg/kg bw/day) (95th percentile)	Average consumers (µg/kg bw/day)	High consumers (µg/kg bw/day) (95th percentile)	Average consumers (µg/kg bw/day) (95th percentile)	High consumers (µg/kg bw/day)	Average consumers (µg/kg bw/day)	High consumers (µg/kg bw/day) (95th percentile)
35								
36	#WAAARDE!	#WAAARDE!	#WAAARDE!	#WAAARDE!	#WAAARDE!	#WAAARDE!	#WAAARDE!	#WAAARDE!
37	#WAAARDE!	#WAAARDE!	#WAAARDE!	#WAAARDE!	#WAAARDE!	#WAAARDE!	#WAAARDE!	#WAAARDE!
38	0,001045	0,0021835	0,014795	0,030913763	0,0006545	0,00154	0,009266342	0,021803158
39	0,0004015	0,000869	0,005684395	0,012303211	0,0002145	0,000451	0,003036868	0,006385211
40	0,0003465	0,000726	0,004905711	0,010278632	0,000231	0,000561	0,003270474	0,007942579
41	#WAAARDE!	#WAAARDE!	#WAAARDE!	#WAAARDE!	#WAAARDE!	#WAAARDE!	#WAAARDE!	#WAAARDE!
42	#WAAARDE!	#WAAARDE!	#WAAARDE!	#WAAARDE!	#WAAARDE!	#WAAARDE!	#WAAARDE!	#WAAARDE!

Figure 5: Outcome of the acute and chronic exposure assessment for T2 and HT-2 toxin in oat bran in the Belgian population, using available consumption data of 'other children', 'adolescents' and 'adults'.

## 2.4 Risk characterization

Risk characterization is defined as an estimation of the probability of occurrence and severity of known or potential adverse health effects in a population. It comes down to comparing the outcome of the exposure assessment with a certain threshold value from previous hazard characterization. The methodology differs depending on the type of hazard (genotoxic carcinogen or non-genotoxic compound).

For acute exposure, the outcome of the exposure assessment is compared with the ARfD. If the exposure exceeds this dose, there is a potential risk identified. The tool calculates the hazard quotient (HQ), which is nothing more than the exposure value divided by the ARfD. If this is larger than 1, it means that the exposure value exceeds the ARfD, and a certain risk is identified. The tool generates a red color when a risk is identified.

A similar methodology is applied for chronic exposure to non-genotoxic compounds. The outcome of the exposure assessment is compared with the chronic HBGV or TTC. If the exposure exceeds this value, there is a potential risk identified. The tool calculates the HQ, which is the quotient of the exposure value and the HBGV. If this is larger than 1, it means that the exposure value exceeds the HBGV, and a certain risk is identified. The tool generates a red color when a risk is identified.

For genotoxic carcinogens, it is recommended to work with margins of exposure (MOE), rather than hazard quotients. The MOE is the ratio calculated by determining a level of exposure in which harm to human health is not expected to occur (e.g. BMDL<sub>10</sub>), and then dividing that by an estimated level of human exposure. For genotoxic carcinogens, a value above 10.000 is considered as low risk. When the obtained value is smaller than 10.000, it means that the outcome lies too close to the level at which harm can occur and a potential risk is identified. The MOE is not a HBGV, i.e. it is not a safety threshold below which the daily intake is

considered as safe. When there is evidence of harmful effects but not enough to confirm how much is safe, the MOE tells us if current intakes are likely to be harmful or not: a low MOE represents a greater risk than a higher MOE.

For completeness, note that a MOE can also be used for non-genotoxic compounds when there are too many uncertainties to establish a HBGV. Usually, a BMDL<sub>10</sub> or a NOAEL is then used. The MOE should generally be higher than 100 or 1000 to imply a low risk, depending on the type of contaminant. These calculations are not included in the tool, but can be easily done by inserting the BMDL<sub>10</sub> or NOAEL in the cell of genotoxic carcinogens (cell B5), and interpret the MOEs accordingly in the risk characterization. However, the cells will turn red when the obtained values are lower than 10.000, but keep in mind that they should now be lower than 100-1000 to indicate a potential risk. This should be evaluated on a case-by-case basis.

### Example

In this example, we will characterize the risk related to the exposure to the sum of T2 and HT-2 after consumption of oat bran by the Belgian population.

By now, every required information is inserted in the tool. As described above, we will work with the ARfD of 0.3 µg/kg bw/day for acute exposure and the TDI of 0.02 µg/kg bw/day for chronic exposure. We will now evaluate if the obtained exposure values exceeds these reference values or not. If there is exceedance, then there is a potential risk identified.

Let's look at acute exposure first. As derived from the tool (Figure 5), the acute exposure ranges between 0,0003 and 0.0309 µg/kg bw/day throughout all available age categories, consumption patterns and scenarios. At a first glance, we see already that no value exceeds the ARfD of 0.3 µg/kg bw/day. Therefore no potential risk after acute exposure is identified with the available data. This is confirmed by the tool at the risk characterization step (Figure 6); where no HQ of >1 was calculated, hence no cell turned red for potential risk indication.

4. RISK CHARACTERIZATION				
Non-genotoxic ACUTE HQ = Exposure/ARfD				
	LB MEAN CONCENTRATION		UB mean CONCENTRATION	
	Average consumers (µg/kg bw/day)	High consumers (µg/kg bw/day) (95th percentile)	Average consumers (µg/kg bw/day)	High consumers (µg/kg bw/day) (95th percentile)
48 Infants 0-11 months	#WAARDE!	#WAARDE!	#WAARDE!	#WAARDE!
49 Toddlers 12-35 months	#WAARDE!	#WAARDE!	#WAARDE!	#WAARDE!
50 Other children 36 months-9 years	0,003483333	0,007278333	0,049316667	0,103045877
51 Adolescents 10-17 years	0,001338333	0,002896667	0,018947982	0,041010702
52 Adults 18-64 years	0,001155	0,00242	0,016352368	0,034262105
53 Elderly 65-74 years	#WAARDE!	#WAARDE!	#WAARDE!	#WAARDE!
54 Very elderly 75 years and older	#WAARDE!	#WAARDE!	#WAARDE!	#WAARDE!

Figure 6: Outcome of the risk characterisation of T2 and HT-2 toxin in oat bran in the Belgian population, after acute exposure. The cells where data were available turned green, indicating no risk.

For chronic exposure, the calculations are similar, but now, the TDI is used. As T2 and HT-2 toxin are not on the list of genotoxic carcinogens, the tool will not calculate the MOE (because cell B5 is empty), but a HQ. The chronic exposure ranges from 0.0002 to 0.0218 µg/kg bw/day (Figure 5). At the first glance, we see that in the category of 'other children', the TDI is exceeded in the upper bound scenario of high consumers. Remember, the upper bound scenario replaces values below LOQ with the LOQ. As 36 of 38 samples were below LOQ, this scenario is very likely an overestimation. However, this a nice illustration of how the tool can identify potential risks related to chemicals in food. The risk characterization step of the tool confirms a HQ > 1 for high-consuming children between 3 and 9 years old at the upper bound scenario, indicating a potential risk by turning red (Figure 7).

Non-genotoxic compounds HQ = chronic exposure/HBGV				
	LB MEAN CONCENTRATION		UB MEAN CONCENTRATION	
	Average consumers (µg/kg bw/day)	High consumers (µg/kg bw/day) (95th percentile)	Average consumers (µg/kg bw/day)	High consumers (µg/kg bw/day) (95th percentile)
69				
70	#WAARDE!	#WAARDE!	#WAARDE!	#WAARDE!
71	#WAARDE!	#WAARDE!	#WAARDE!	#WAARDE!
72	0,032725	0,077	0,463317105	1,090157895
73	0,010725	0,02255	0,151843421	0,319260526
74	0,01155	0,02805	0,163523684	0,397128947
75	#WAARDE!	#WAARDE!	#WAARDE!	#WAARDE!
76	#WAARDE!	#WAARDE!	#WAARDE!	#WAARDE!
77				

Figure 7: Outcome of the risk characterisation of T2 and HT-2 toxin in oat bran in the Belgian population, after chronic exposure. The cells where data were available turned green, except for the category 'other children', in the upper bound scenario of high consumes, indicating a potential risk.

We are now at the end of the risk assessment. If you notice that many values are exceeding the reference values, it is of importance to further finetune the risk assessment with more advanced probabilistic calculations. These calculations will take into account the whole distribution of a population, rather than point estimates, and will give an outcome reflecting better the realistic circumstances. Nevertheless, this toolkit is useful for a basic understanding of risk assessment, and to get acquainted with the methodology.

### 3 Concluding remarks and further reading

Thank you for completing this manual for the risk assessment toolkit. Both the use of the data collection format and the risk assessment tool were described as briefly as possible. Please find all necessary files on the FoodSafety4EU platform. The files will be updated according to changes or user feedback.

For more elaborate explanation on chemical risk assessment, please consider following resources:

FAO/WHO, 2009. Principles and Methods for the Risk Assessment of Chemicals in Food. Environmental Health Criteria 240. 752 pp.  
[https://apps.who.int/iris/bitstream/handle/10665/44065/WHO\\_EHC\\_240\\_eng.pdf](https://apps.who.int/iris/bitstream/handle/10665/44065/WHO_EHC_240_eng.pdf)

EFSA, 2005. Opinion of the Scientific Committee on a request from EFSA related to A Harmonised Approach for Risk Assessment of Substances Which are both Genotoxic and Carcinogenic. EFSA Journal, 282, 1-31.  
<https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2005.282>

EFSA, 2007. Opinion of the Scientific Committee related to Uncertainties in Dietary Exposure Assessment. EFSA Journal, 438, 1-54. <https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2007.438>

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EFSA, 2010. Standard sample description for food and feed. EFSA Journal, 8(1):1457.  
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EFSA, 2012. Scientific Opinion on Risk Assessment Terminology. 10(5):2664. <https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2012.2664>

EFSA, 2017. Update: use of the benchmark dose approach in risk assessment. EFSA Journal, 15(1):4658. <https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2017.4658>

EFSA, 2019. Guidance on the use of the Threshold of Toxicological Concern approach in food safety assessment. 17(6):5708. <https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2019.5708>



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