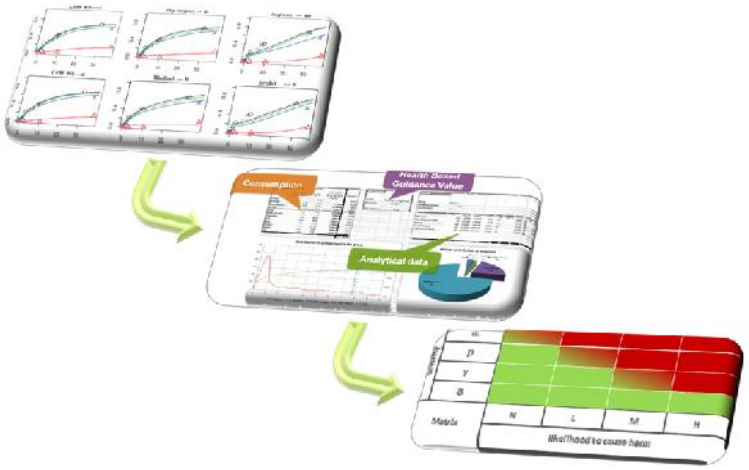

Research

Impact of Hazard Characterization Methodology on the Management of MCPD- and Glycidyl Esters in Food Raw Materials

DFG symposium on ME and GE
20.-21. June 2017, Berlin

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Overview

- Problem formulation
- Nestlé approach to integrate Risk Assessment in the management of chemical contaminants in raw materials
- Example of 3-MCPD
- Conclusions

Research

Risk assessment of 3-MCPD-esters (ME)

According to the general RA paradigm

- ME were identified in vegetable fats & oils (palm oil)
- Database on levels mainly in vegetable fats and oils
- Humans are exposed via food
- ME ('bound') are a source of exposure to MCPD ('free')

- 3-MCPD is toxic to kidney and testes in rodents
- Non-genotoxic (threshold mechanism)
- Dose response characterisation available
- Health Based Guidance Value(s) established (TDI)

- Human exposure may exceed TDI in certain populations, particularly formula-fed infants

➢ ***Need to manage***

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Problem formulation

Risk assessment

- RA authorities (EFSA, JECFA, other)
- Occurrence database
- Consumer total dietary exposure
- Toxicity - Safe levels of exposure
- Risk of exceeding safe exposure levels in populations / sub-populations
- Based on 'numbers'

translation

➢ *Population focus*

Quality management

- Ensure compliance with legal limits (raw materials) set by Regulatory authorities (EC, codex, national…) - *if available*
- Specifications (RMPS)
- Process control (HACCP)
- Originally based on 'hazard'

➢ *Supply chain focus (raw materials)*

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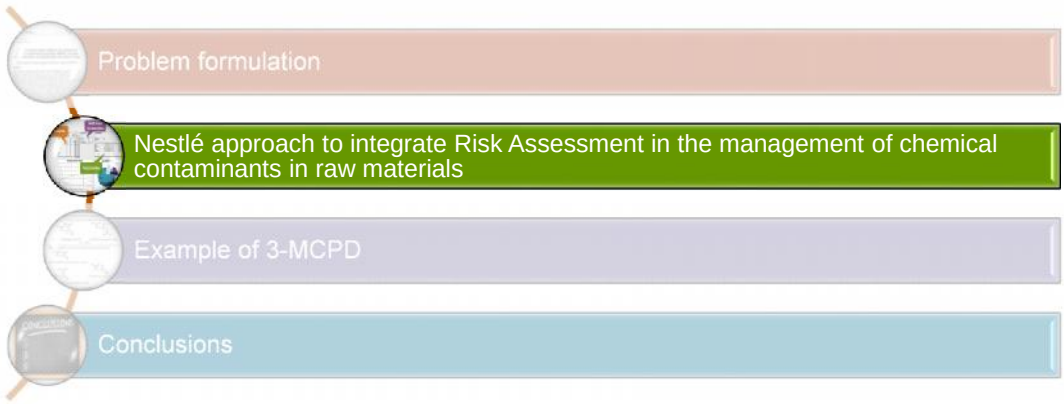


Objective

Nestlé global approach

To define a global, harmonised ap… …to manage chemical contaminants in raw materia… …sound and defendable

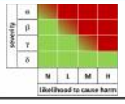
pragmatic

- Global
- Raw materials
- Scientific risk assessment principles

Output: Tool for the prioritisation of chemicals to h… materials, entailing the use of decision tr…

Compatible with existing processes (HACCP)

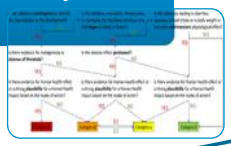
- Severity
- Risk (likelihood to cause harm)



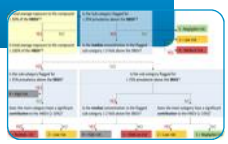
Risk Assessment

General paradigm

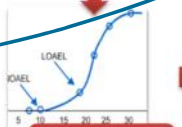
Assessing *severity*



Assessing *risk*



Hazard identification
- Toxicity
- Epidemiology
- Outbreaks



Hazard characterisation
- Dose response
- Safe level of exposure

Risk characterisation
- Probability
- Severity

Occurrence
- Analytical data
- Limits

Exposure
- Food consumption
- Other sources of exposure

Risk management:
- Decision - Action plan - Verification

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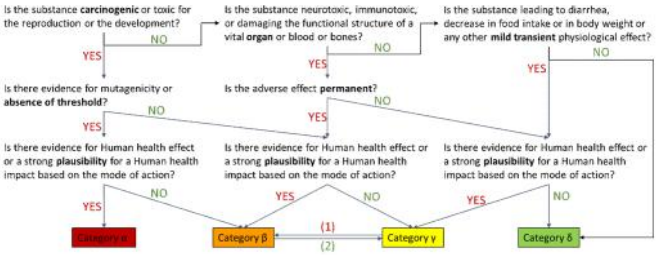
Severity

Hazard identification
- Toxicity
- Epidemiology
- Outbreaks

Decision tree



Criteria for setting the severity (decision tree)

- Chronic exposure (not acute), oral route (not inhalation or injection)
- Carcinogenicity, reproductive and developmental toxicity
- Structural changes/ functional damage in critical organs or systems
- Mutagenicity/ absence of a threshold
- Reversibility
- Evidence in humans/ plausibility for human effect

➢ Categorisation into ~, , ¥, ¢ (most severe - least severe)

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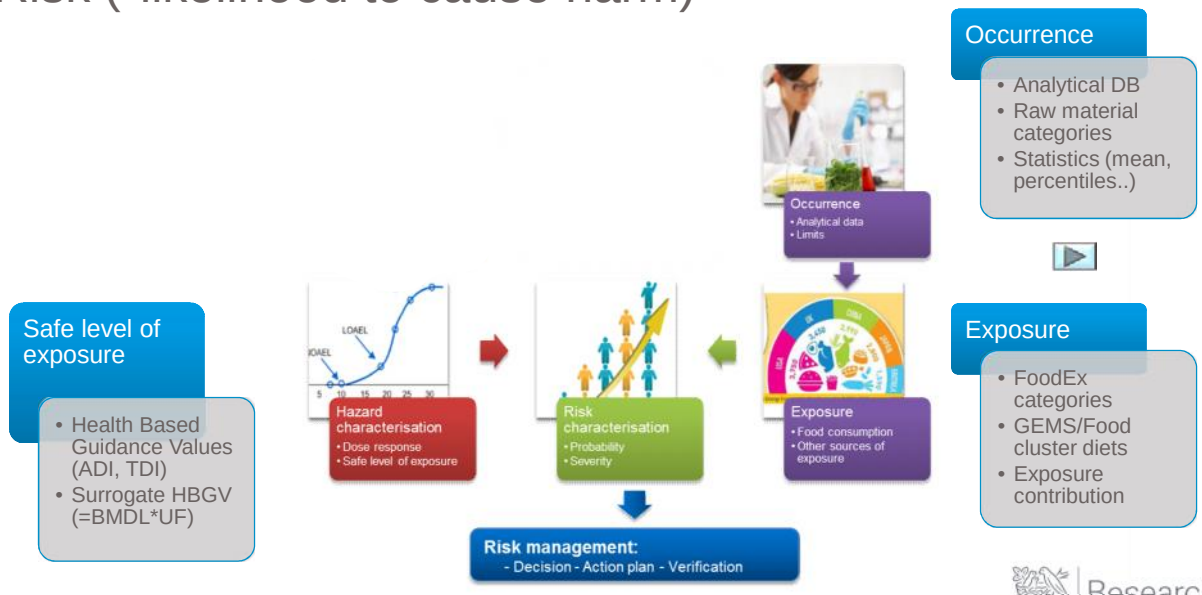
Risk (*likelihood to cause harm)



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Raw Material Categorisation

- Alignment with WHO GEMS/Food Cluster diets, EU FoodEx categorisation
- Global food intake scenario (weighted average across all cluster diets)

	groups	intake (g)	1	2	3	4	5	6	7
1	Grains	353	Wheat	Rye	Oats	Corn	Rice	Barley	Others
2	Seeds and roots	193	Nuts	Leguminous seeds	Oilseeds	Starchy roots			
3	Vegetables	265	Brassica vegetables	Fruiting vegetables	Leafy, stalk and stem vegetables	Bulb and root vegetables	Legume vegetables	Other vegetables	
4	Fruit	197	Berries and other small fruits	Citrus fruits	Pome fruits	Stone fruits	Tropical and subtropical fruits	Other fruits	Heat processed fruits
5	Dairy	151	Milk (raw, processed and powder)	Whey & other milk derivates	Cheese	Yoghurt	Butter Milk	Cocoa & Malt beverages	Lactose
6	Proteins	159	Mammals	Eggs & Eggs derivates	Poultry	Fish & Sea food	Vegetable proteins		
7	Sweets	72	Sugars, candies	Cocoa & its non-liquid derivate	Chocolate and chocolate equivalent	Honey			
8	Fats	38	Vegetable fats & Oils	Terrestrial animal fats (incl. poultry fats)	Marine animal fats	Milk fat			
9	Miscellaneous	35	Seasonings (spices, herbs, & condiments)	Sauces, savories & vinegar	Miscellaneous agents for food processing	Additives, flavorings, sweeteners & coloring agents	Vitamins and minerals		
10	Beverages	2000	Water	Fruit & vegetable juices	Coffee	Tea	Coffee substitutes		

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Issue: Translation of HBGVs (TDI, ADI) into Safe Levels in Raw Materials

Definition of TDI (EFSA glossary)

- The tolerable ***daily*** intake (TDI) is an estimate of the amount of a substance in ***food or drinking water*** which is not added deliberately (e.g contaminants) and which can be consumed over a lifetime without presenting an appreciable risk to health.

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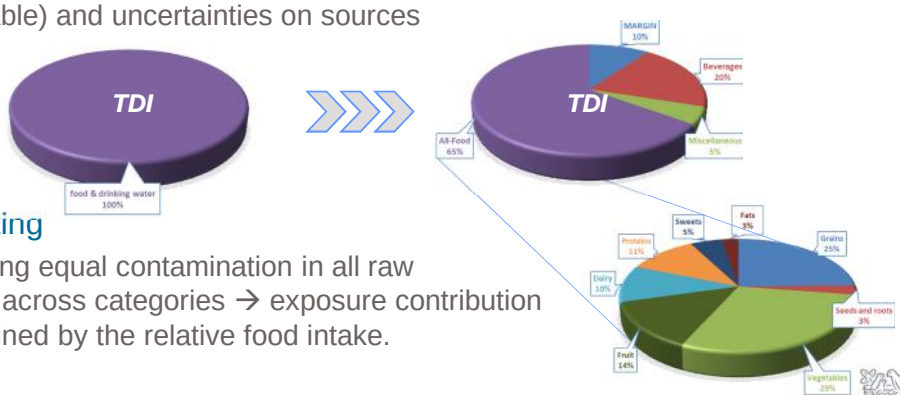
Issue: Translation of HBGVs into Safe Levels in Raw Materials

Quota concept

- Allocate fractions of the TDI to raw material categories and beverages
- Additional margin for other sources of exposure (environmental) or process formation (if applicable) and uncertainties on sources



Default setting

- Considering equal contamination in all raw materials across categories → exposure contribution is determined by the relative food intake.

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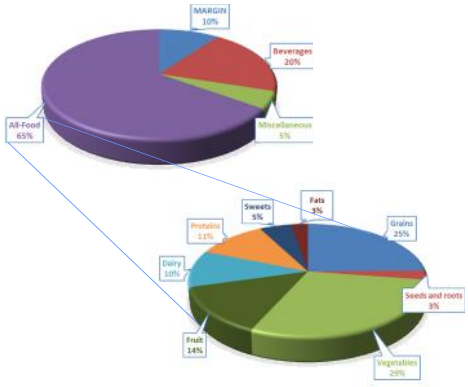
Issue: Translation of HBGVs into Safe Levels in Raw Materials

Quota concept:

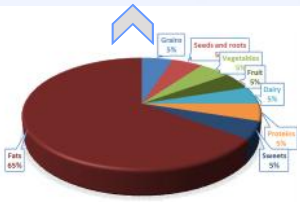
- Allocation of fractions of the TDI to the different RM categories, based on available knowledge on occurrence (or absence) in the different categories



***S**afety **B**ased **G**uidance **V**alues (SBGV)*

Calculated based on:

- *% fraction of the TDI*
- *Dietary consumption of RM category*
- *Body weight of 60 kg (adult)*



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Safety Based Guidance Value (SBGV)

Definition:

The **SBGV** refers to the level of a given chemical in a specific food raw material (**expressed in mg/kg of raw material**) consumed in the context of an average global diet, that can be ingested (orally) on a daily basis over a lifetime without an appreciable health risk.

Exceedance of this level does not necessarily imply a health risk. A case by case investigation is required to assess the actual risk (based on exposure scenarios, specific population/consumer groups, local circumstances etc.)

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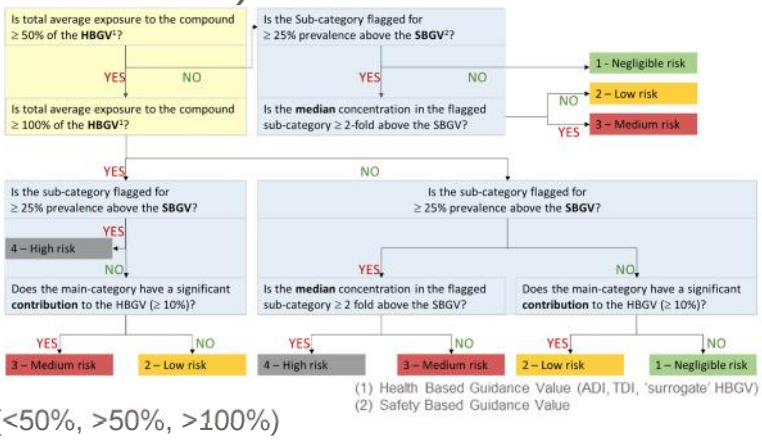
Risk (likelihood to cause harm)

Decision tree

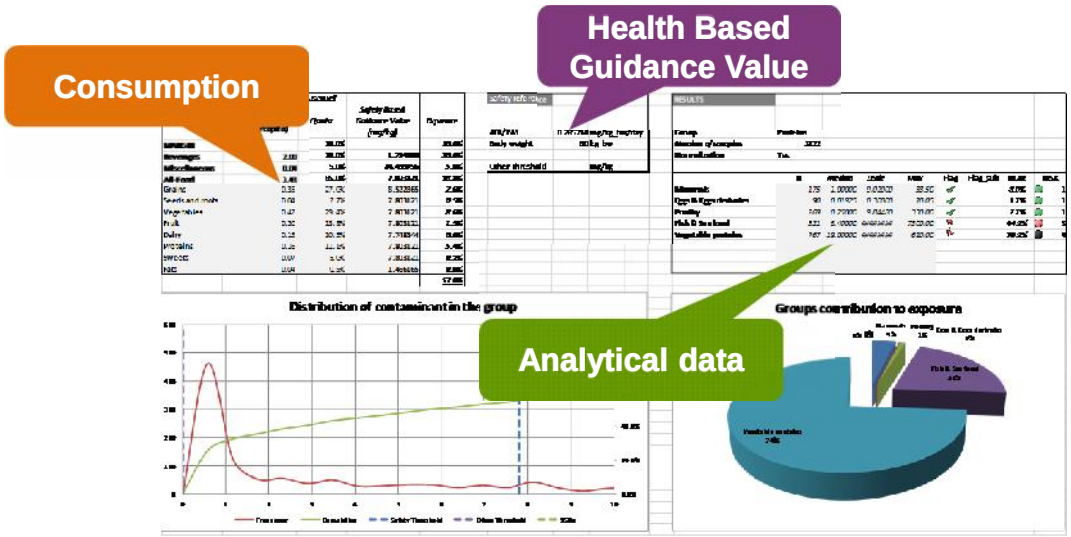
- Used to set the level of risk
- Categories:
  (**N**) negligible
  (**L**) low
  (**M**) medium
  (**H**) high



Based on

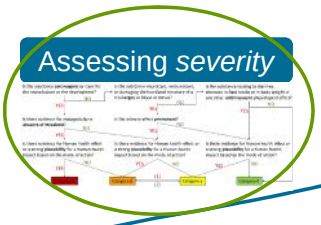
- Level of exhaustion of **HBGV** (<50%, >50%, >100%)
- Frequency of exceeding the **SBGV** (cut-off 25%) → 'occurrence flag'
- Numerical **median** concentration value (>2x SBGV)
- Significant exposure **contribution** to HBGV (>10% of HBGV)

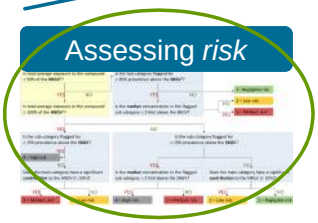
Risk Assessment Tool



Risk Assessment

General paradigm





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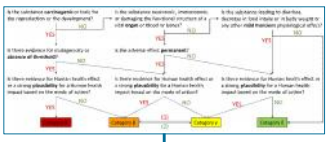
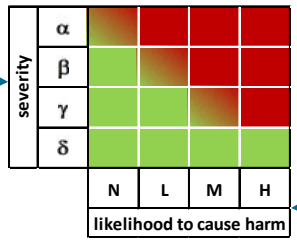
Significance Matrix

Combination of Severity x Risk (from decision trees)

- For any combination of contaminant x raw material
- Trigger investigation
  - Local assessment
  - Analysis
  - Mitigation…
- Consideration in:
  - HACCP studies
  - Surveillance/ monitoring programs
  - Raw material purchasing specifications





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3-MCPD – Health Based Guidance Values

Summary of hazard characterisations by authorities

- Based on the assumption of full hydrolysis of esters in the GI tract

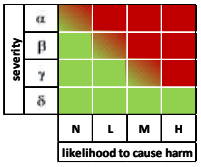
**10x10 for *inter*- and *intra*species variability

Evaluation	Tox basis	Tox endpoint	BMDL10 (mg/kg bw/d) (*LOEL)	UF**	Uncertainty	TDI (µg/kg bw/d)
JECFA, 2001 & 2007	Sunahara et al., 1993	Tubular hyperplasia	1.1*	500	LOEL → NOEL	2
EC SCF, 2002	Sunahara et al., 1993	Tubular hyperplasia	1.1*	500	Lack of repro-/ developmental tox	2
EFSA, 2016	Cho et al., 2008	Tubular hyperplasia	0.077	100	--	0.8
JECFA, 2016	Cho et al., 2008	Tubular hyperplasia	0.87	200	Inadequacy of reprotox studies	4

Example of 3-MCPD

Elements required

Severity (gamma)



Risk

- HBGV: TDI **0.8** or **4 µg/kg bw/day** (EFSA vs JECFA)
- Repartition of the TDI to raw material categories (definition of 'quota')
- 'Risk Assessment Tool'
  - Calculation of **Safety Based Guidance Values**
  - Determination of exposure and **risk** based on occurrence data (internal database)

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Safety Based Guidance Values

According to the TDI used

	'Quota' (% of TDI)	SBGV (µg/kg)	SBGV (µg/kg)	SBGV (µg/kg)
Miscellaneous (incl. soy sauce)	3 %	40	100	205
Fats & oils (all)*	43.6 %	**550**	**1375**	**2750**

** Applicable to all edible fats & oils (from vegetable and animal sources), global / average / adult intake scnario*

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Practical consequences

Analytical data distribution

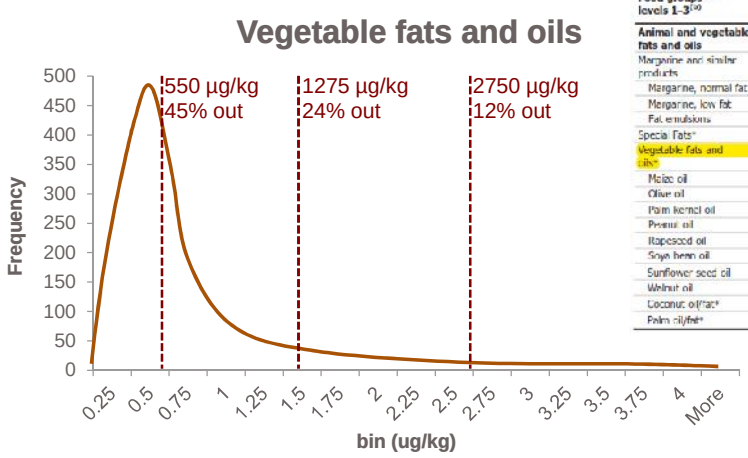


Table 11: Mean, median and 95th percentile of concentrations (µg/kg) of 3-MCPD (from esters) in food groups related to the Comprehensive Food Consumption groups (including some *ad hoc* ones) in the data set on fats and oils

Food groups[a,b] levels 1–3[c,d]	N[e]	% LC[e]	LOQ (min-max) (µg/kg)	Mean[e,f] MB (LB–UB) (µg/kg)	Median[e,f] MB (LB–UB) (µg/kg)	P95[e,f] MB (LB–UB) (µg/kg)
Animal and vegetable fats and oils	2,150	5	(13–150)	1,034 (1,032–1,037)	490	3,000
Margarine and similar products	170	2	(16–150)	406 (406–409)	244 (240–246)	1,150
Margarine, normal fat	73	–	(16–150)	668 (667–668)	430	1,640
Margarine, low fat	82	4	(22–100)	216 (215–220)	100 (177–100)	430
Fat emulsions	15	–	(50–100)	181	150	–
Special fats*	41	–	(100–130)	867	750	–
Vegetable fats and oils*	1,939	5	(13–150)	1,093 (1,090–1,095)	510	4,020
Maize oil	38	3	(100–150)	503 (502–505)	430	–
Olive oil	9	11	13	48 (48–49)	37	–
Palm kernel oil	37	–	(100–150)	625	500	1,410
Peanut oil	8	–	(13–150)	229	235	–
Rapeseed oil	297	16	(100–150)	232 (224–239)	180	630
Soya bean oil	191	4	(100–150)	394 (392–396)	330	914
Sunflower seed oil	506	7	(50–150)	521 (517–524)	410	1,510
Walnut oil	1	–	13	236	–	–
Coconut oil/fat*	854		(100–150)	608	590	1,050
Palm oil/fat*	301	< 1	(100–150)	2,912	2,920	5,210

EFSA, 2016

Action triggered

Analytics

- Method development
- Data generation

Enagagement with suppliers

- Understanding formation
- Mitigation studies
- Communication of objectives with suppliers

Monitoring

Conclusions I

Development of a tool that allows to integrate risk assessment in the management of chemical contaminants

- Results are consistent with published information (exposure, severity, risks)
- Globally applicable to all kinds of chemical contaminants, not only 3-MCPD (flexibility)
- Outcome is used as an input to management of chemical contaminants (justification for monitoring, mitigation, investigation, HACCP studies, setting of specifications…)

Limitations

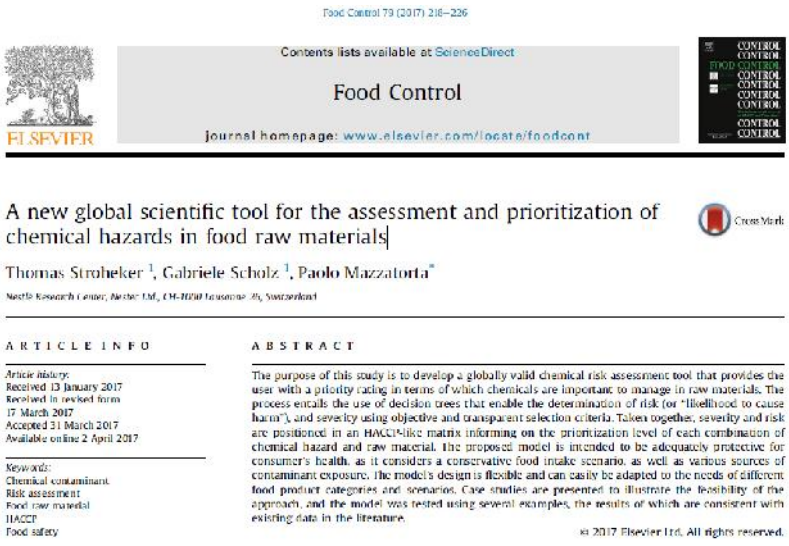
- Limited applicability to process related contaminants (if not occurring in RMs)
- Currently out of scope: small children, allergens, packaging materials

Conclusions II

3-MCPD:

- Need for clear messages from the risk asessment, alignment between authorities (globally defendable)
- Clear messages from risk management that are coherent with the outcome of the risk assessment
- Need for clear messages to our businesses and markets (to justify management action)
- Safety Based Guidance Values would be compatible with anticipated limits in vegetable fats and oils

Publication



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A new global scientific tool for the assessment and prioritization of chemical hazards in food raw materials

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ABSTRACT

The purpose of this study is to develop a globally valid chemical risk assessment tool that provides the user with a priority rating in terms of which chemicals are important to manage in raw materials. The process entails the use of decision trees that enable the determination of risk (or "likelihood to cause harm"), and severity using objective and transparent selection criteria. Taken together, severity and risk are positioned in an HACCP-like matrix informing on the prioritization level of each combination of chemical hazard and raw material. The proposed model is intended to be adequately protective for consumer's health, as it considers a conservative food intake scenario, as well as various sources of contaminant exposure. The model's design is flexible and can easily be adapted to the needs of different food product categories and scenarios. Case studies are presented to illustrate the feasibility of the approach, and the model was tested using several examples, the results of which are consistent with existing data in the literature.

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Project team

Nestle Research Center

- Paolo Mazzatorta ('TOP' Project Manager)
- Thomas Stroheker
- Gabriele Scholz
- Benoît Schilter

Nestlé Quality Management

- Pascal Volery
- Richard Stadler

Chemical contaminant experts in Nestlé Product Technology Centers and Quality Assurance Centers

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Thank you for you kind attention !

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backup

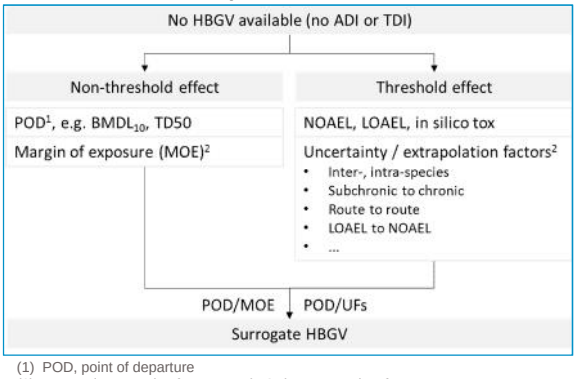
Health Based Guidance Values

HBGV

- Established by competent authorities (JECFA, EFSA…)
- Most comprehensive, global, recent

Surrogate HBGV (sHBGV)

- In absence of HBGV
- Depending on type of effect (threshold or not)



(1) POD, point of departure
(2) Appropriate margin of exposure (MOE) or uncertainty factor (UF) associated with low concern for human exposure

Glycidol

Summary of hazard characterisations by authorities

- Based on the assumption of full hydrolysis of esters in the GI tract

Evaluation	Tox basis	Tox endpoint	$BMDL_{10}$ (mg/kg bw/d)	MOE	Exposure level of 'low concern' (µg/kg bw/d)
BfR, 2009	NTP, 1990	Peritoneal mesothelioma	T25 = 10.2 BMD10 = 4.1	25'000 10'000	0.41
EFSA, 2016	NTP, 1990	Peritoneal mesothelioma	T25 = 10.2	25'000	0.41
JECFA, 2016	NTP, 1990	Peritoneal mesothelioma	$BMDL_{10}$ = 2.4*	10'000	0.24

* EPA BMD model