

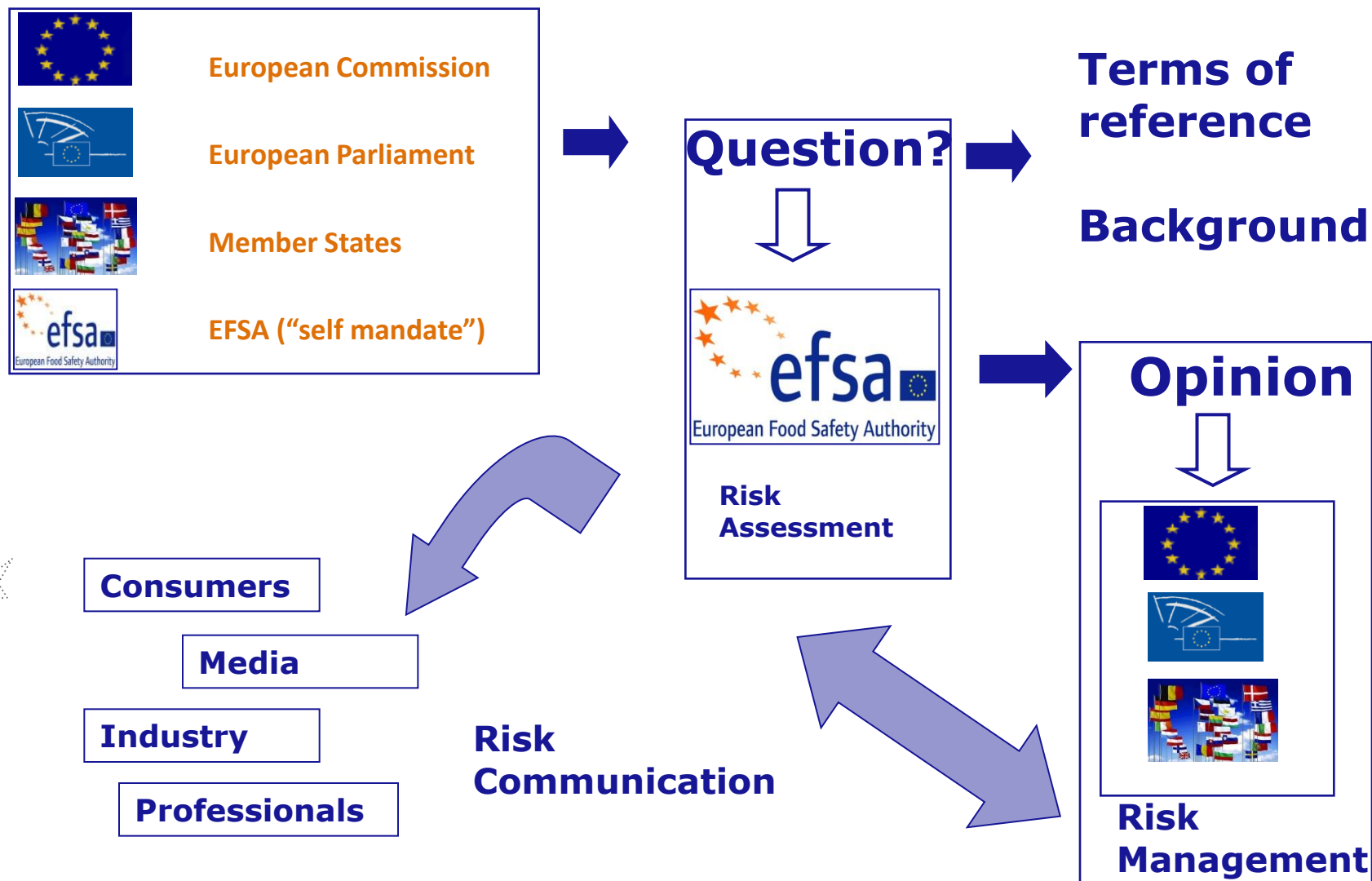


OpenFoodTox and Other Open Source *In silico* Tools @ EFSA

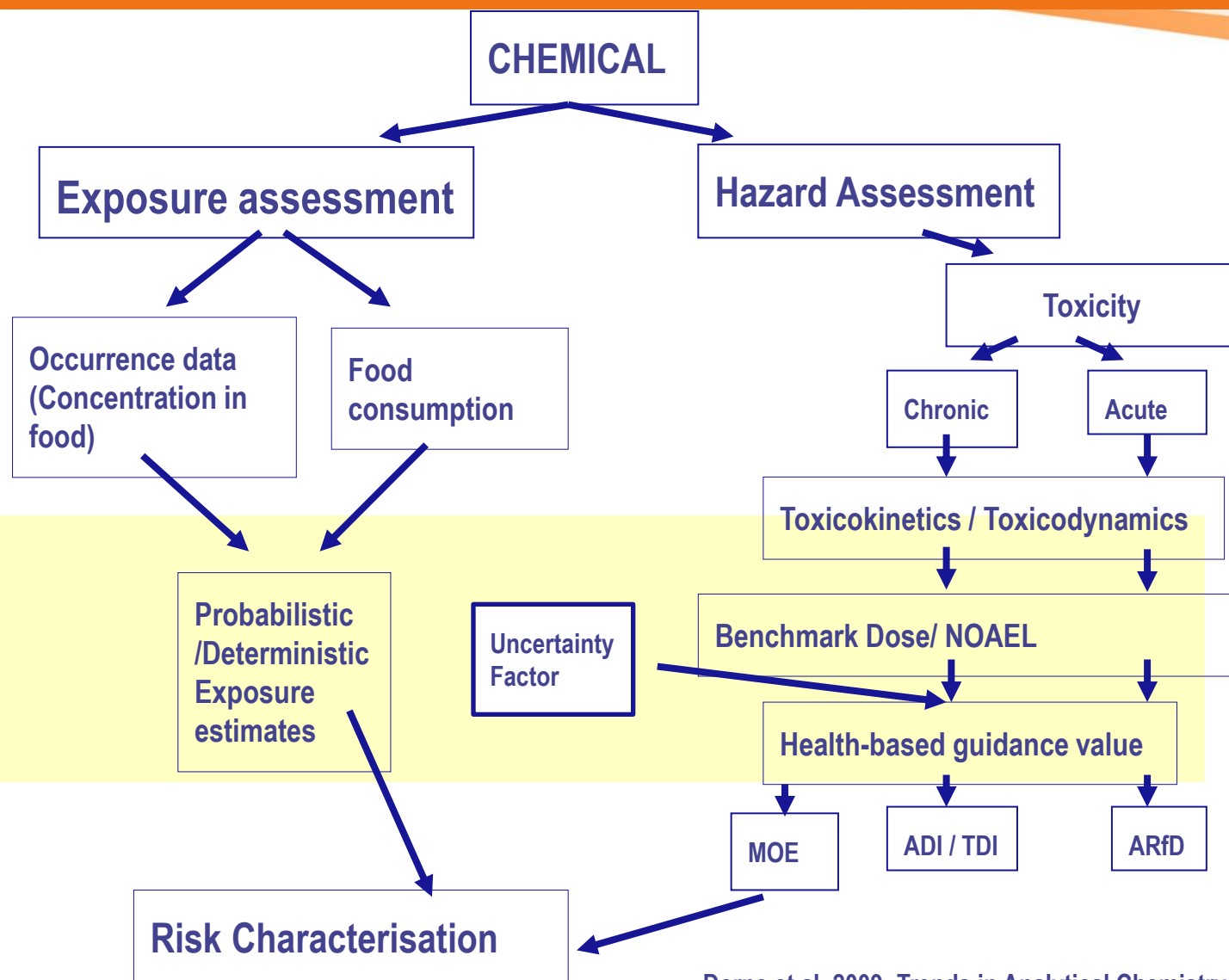
Jean Lou Dorne
Senior Scientific Officer
Scientific Committee and Emerging Risks Unit
EFSA

EFSA FCM Network 10th July 2017

FROM QUESTION TO ANSWER



IN A NUTSHELL...





EDITORIAL



APPROVED: 26 March 2015

PUBLISHED: 27 March 2015

doi:10.2903/j.efsa.2015.e13031

Increasing robustness, transparency and openness of scientific assessments

**Hardy A, Dorne JLCM, Aiassa E, Alexander J, Bottex B,
Chaudhry Q, Germini A, Nørrung B, Schlatter J, Verloo D,
Robinson T**

OUTPUT CATEGORY

ADOPTED:

doi:10.2903/j.efsa.20YY.NNNN

Guidance on The Use of the Weight of Evidence Approach in Scientific Assessments

EFSA Scientific Committee,

Maged Younes (Chair), Jan Alexander, Emilio Benfenati, Qasim Mohammad Chaudhry, Peter Craig, Geoff Frampton, Matthias Greiner, Tony Hardy, Andrew Hart, Christer Hogstrand, Claude Lambre, Robert Luttik, David Makowski, Alfonso Siani, Christian Gortazar Schmidt, Helene Wahlstroem, Jaime Aguilera, Jean-Lou Dorne, Laura Martino, Nikolaos Georgiadis

DATA/EVIDENCE AVAILABLE IN CHEMICAL RA

Tier	Exposure Assessment		Hazard identification		Hazard characterisation		Risk Characterisation
	Occurrence	Consumption	TK	TD	TK	TD	
0	Semi-Q	Default values	No data	No data	<i>in silico</i> Read across	Default values TTC Read across <i>In silico</i> Default UF	e.g. Default values Qualitative
1	Point estimates	Point estimates in food categories	<i>In silico</i> Limited data Semi-Q	<i>In silico</i> Limited data Read across	<i>in silico</i> Basic TK Read across	<i>in silico</i> Read across NOAEL Default UF	e.g. Semi-quantitative
2	Measured data	Measured in some food categories	Dossier data Qttve	Dossier Data	<i>in silico</i> ADME data	NOAEL/ BMDL Default <i>in silico</i> UF	e.g. Quantitative Deterministic/ Probabilistic
3	Large measured dataset	Full patterns - food categories	Dossier and/or lit. (<i>in vitro</i> , <i>in vivo</i>)	Data dossier and/or lit. (<i>in vitro</i> , OMICs, epi)	MoA/AOP, Epi data, PB-PK model, BBDR, BMDL Chemical adjustment (CSAF)	specific factor	e.g. Quantitative Full probabilistic

DATA FROM DOSSIER: REGULATED PRODUCT

Tier	Exposure Assessment		Hazard identification		Hazard characterisation		Risk Characterisation
	Occurrence	Consumption	TK	TD	TK	TD	
2	Measured data	Measured in some food categories	Dossier data Qttve	Dossier Data: genotox, tox	<i>in silico</i> ADME data	NOAEL/ BMDL Default UF	e.g. Quantitative Deterministic/ Probabilistic

DATA-RICH CHEMICAL: CADMIUM

Tier	Exposure Assessment		Hazard identification		Hazard charact		Risk Characterisation
	Occurence	Consumption	TK	TD	TK	TD	
3	Large measured dataset	Full patterns - food categories	Human Data Biomarker excretion/ blood	Human data Biomarker renal toxicity	PB-PK-BMDL (Human data) Chemical specific adjustment factor (CSAF)		e.g. Quantitative Full probabilistic

DATA-POOR: EMERGING MYCOTOXIN

Tier	Exposure Assessment		Hazard identification		Hazard characterisation		Risk Characterisation
	Occurrence	Consumption	TK	TD	TK	TD	
0	Semi-Q	Default values	No data	No data	<i>in silico</i> Read across	Default values TTC Read across <i>In silico</i> Default UF	e.g. Default values Qualitative



OpenFoodTox: EFSA's Open Source Hazards Database

EDITORIAL

APPROVED: 8 December 2016

doi: 10.2903/j.efsa.2017.e15011

Editorial: OpenFoodTox: EFSA's open source toxicological database on chemical hazards in food and feed

**Jean Lou Dorne^a, Jane Richardson^b, Georges Kass^a, Nikolaos Georgiadis^c,
Mario Monguidi^d, Luca Pasinato^d, Stefano Cappe^e, Hans Verhagen^f and
Tobin Robinson^g**

OPENFOODTOX: EFSA' S CHEMICAL HAZARDS DATABASE

■ Catalogue of EFSA's chemical toxicity data since creation

- Contaminants (Human and Animal health)
- Vitamins and minerals (Human health) (NDA),
- Food additives and Nutrient Sources, Food contact materials, Flavourings and processing aids (Human Health)
 - Feed Additives (Human and Animal Health, Ecotoxicology)
- Pesticides (Human and Animal health, Ecotoxicology)

■ Easy Reference and Crisis

- One reference DB Chemical Hazards: Search easily and efficiently
- Crisis: Quick and Easy access to all EFSA's Hazard Data

■ International Harmonisation

- Use OECD Harmonised Templates (OHT) for data model (ECHA/OECD) compatible with IUCLID/ ECHA-OECD QSAR toolbox
- Search compounds by name, CAS number on e-chem portal
- Generate data sheet as summary of hazard id and charact (June 2016)

WHAT DOES OPENFOODTOX CONTAIN ?

○ Chemical Information

Information on chemical nomenclature (EU nomenclature, IUPAC, CAS...), trade name, chemical group/panel (i.e. pesticide), chemical use (i.e. fungicide), chemical structure (i.e. triazoles, organophosphates...).

○ Document descriptors

Information on EFSA's opinion for the specific chemical or group of chemicals. Info from EFSA 's RAW system (question number, mandate, number), link to the document

○ Toxicity Endpoint/ Hazard identification

Information on critical toxicity study using OECD picklists when possible (species, dose, target organ...)

○ Critical study to demonstrate genotoxicity status

Providing essential information of critical genotoxicity study when assessed

○ Hazard /Risk characterisation

Information for health based guidance values (ADI/TDI) uncertainty factors...

TOWARDS AN OPENSOURCE HAZARD DATABASE

Tier	Exposure Assessment		Hazard identification		Hazard characterisation		Risk Characterisation
	Occurrence	Consumption	TK	TD	TK	TD	
0	Semi-Q	Default values	No data	No data	<i>in silico</i> Read across	Default values TTC <i>In silico</i>	e.g. Default values Qualitative
1	Point estimates	Point estimates in food categories	<i>In silico</i> Limited data Semi-Q	<i>In silico</i> data Read across	<i>in silico</i> Basic TK Read across	<i>in silico</i> NOAEL Default UF	e.g. Semi-quantitative
2	Measured data	Measured in some food categories	Dossier data Qttve	Dossier Data	<i>in silico</i> ADME data	NOAEL/BMDL Default <i>in silico</i> UF	e.g. Quantitative Deterministic/ Probabilistic
3	Large measured dataset	Full patterns - food categories	Dossier and/or lit. (<i>in vitro</i> , <i>in vivo</i>)	Dossier and/or lit. (<i>in vitro</i>, OMICs, Epi)	MoA/AOP, Epi data, PB-PK model, BBDR, BMDL, CSAF		e.g. Quantitative Full probabilistic

CONTENT

Microstrategy Tool: <https://dwh.efsa.europa.eu/bi/asp/Main.aspx?rwtrep=400>

Full Download Knowledge junction:

https://zenodo.org/record/344883#.WUDqK_mGPIU

1,650
Scientific
outputs
(metadata +
DOI)

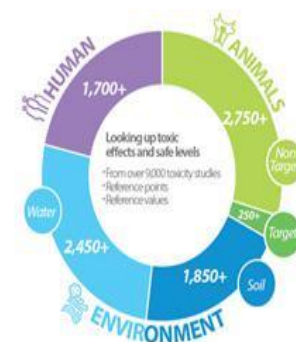
4,400
Substances
(chemical
identifiers
including
SMILES)

10,000
Toxicological
I endpoint
studies

140 Positive
genotoxicity
studies

12,000 risk
assessment
summaries

Use
OpenFoodTox
for



FILTER

Substance Browser

Sub Name (4352)

(All)

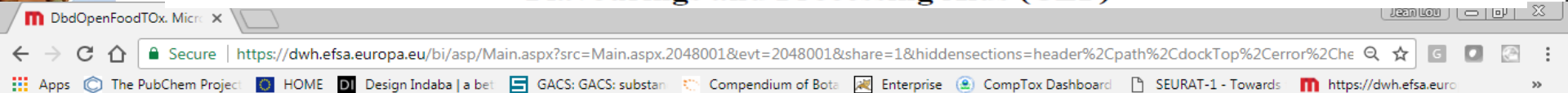
- (-)-3,7-Dimethyl-6-octen-1-ol
- (-)-Alpha-cedrene
- (-)-Alpha-elemol
- (-)-alpha-Santalene
- (-)-Bornyl acetate
- (-)-Hyoscyamine and (-)-Scopolamine group
- (-)-Rhodinol
- (-)-Scopolamine
- ((E)-2-(2-hydroxymethylphenyl)-2-methylpropane-1-carboxamide
- ((2-((2-Ethyl-6-methylphenyl)ethoxy)methyl)-2-ethyl-6-methylphenyl)ethanol
- ((2-((Ethoxymethyl)(2-ethyl-6-methylphenyl)ethoxy)methyl)-2-ethyl-6-methylphenyl)ethanol
- (+)-Alpha-cedrene
- (1R,2R,5S)-5-Isopropenyl-2-methyl-5H-tetralene
- (1R,2R,5S)-Isodihydrocarveol
- (1R,2S,5R)-5-methyl-2-(1-methylethoxy)-5H-tetralene
- (1R,2S,5R)-Menthyl hexanoate
- (1R,2S,5R)-Menthyl salicylate
- (1R,2S,5R)-N-(2-(Pyridine-2-yl)ethyl)-3-p-menthancarboxamide
- (1R,2S,5R)-N-(4-Methoxyphenyl)-3-p-menthancarboxamide
- (1R,2S,5R)-N-((Ethoxycarbonyl)methyl)-3-p-menthancarboxamide
- (1R,2S,5R)-N-Cyclopropyl-3-p-menthancarboxamide
- (1R,2S,5R)-N,N-Dimethyl-3-p-menthancarboxamide
- (1R,2S,5S)-3-Menthoxycarbonyl-3-p-menthancarboxamide
- (1R,2S,5S)-neo-Dihydrocarveol

Substance Characterisation									
Substance		has	Component		CAS Number	EC Ref No	Molecular formula		
(-)-3,7-Dimethyl-6-octen-1-ol		as such	(-)-3,7-Dimethyl-6-octen-1-ol		7540-51-4	231-415-7	C10H20		
(-)-Alpha-cedrene		as such	(-)-Alpha-cedrene		469-61-4	207-418-4	C15H24		
EFSA outputs									
Substance		Output Id	Legal Basis	Panel	Published	Title			
(-)-3,7-Dimethyl-6-octen-1-ol		2180	Commission Regulation (EC)	EFSA CEF	02/20/2013	Scientific Opinion on Flavouring Group Revision 4 (FGE.06Rev4): Straight- and branched-chain aliphatic aldehydes			
Hazard Characterisation: Reference points									
Substance		Author	Year	Output ID	Study	Test Type	Species	Route	Duration (days)
(-)-Hyoscyamine and (-)-Scopolamine group		EFSA CONTAM	2013	2396	Human health	study with volunteers	Human	Not reported	
(1R,2S,5R)-N-(2-(Pyridine-2-yl)ethyl)-3-p-menthanecarboxamide		EFSA CEF	2014	2524	Human health	subchronic	Rat	oral: feed	90
Hazard Characterisation: Reference values									
Substance	Author	Year	Output Id	Assessment	qualifier	value	unit		
(-)-3,7-Dimethyl-6-octen-1-ol	EFSA CEF	2013	2180	TTC Cramer Class I	=	30	µg/kg bw/day		
(-)-Alpha-elemol	EFSA AFC	2006	2232	TTC Cramer Class I	=	30	µg/kg bw/day		
Genotoxicity									
Substance					Author	Year	Output Id	Genotoxicity	
9,10-Dihydroxy stearic acid oligomers					EFSA AFC	2003	344	Not detected	
Acrylic acid, methyl ester, telomer with 1-dodecanethiol, C16-C18 alkyl esters					EFSA AFC	2003	344	Negative	

SCIENTIFIC OPINION

Scientific Opinion on the safety assessment of the substance fatty acids, C16–18 saturated, hexaesters with dipentaerythritol for use in food contact materials¹

EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF)^{2,3}



FILTER

Substance Browser

Sub Name (4352)

dipentaerythritol

Fatty acids, C16-18 saturat...

Substance Characterisation							
Substance	has	Component	CAS Number	EC Ref No	Molecular formula	smiles	
Fatty acids, C16-18 saturated, hexaesters with dipentaerythritol	as such	Fatty acids, C16-18 saturated, hexaesters with dipentaerythritol			C106H216O20-C118H240O20		

EFSA outputs							
	Id					Type	
Fatty acids, C16-18 saturated, hexaesters with dipentaerythritol	2622	Regulation (EC) No 1935/2004 (amended)	EFSA CEF	02/18/2015	Scientific Opinion on the safety assessment of the substance fatty acids, C16-18 saturated, hexaesters with dipentaerythritol for use in food contact materials	EFSA opinion	doi:10.2903/j.efsa.2015.4021

Hazard Characterisation: Reference points

No data returned for this view. This might be because the applied filter excludes all data.

Hazard Characterisation: Reference values

No data returned for this view. This might be because the applied filter excludes all data.

Genotoxicity				
Substance	Author	Year	Output Id	Genotoxicity
Fatty acids, C16-18 saturated, hexaesters with dipentaerythritol	EFSA CEF	2015	2622	Negative

SCIENTIFIC OPINION

Scientific Opinion on the safety assessment of the substance ethylene glycol dipalmitate, CAS No 624-03-3, for use in food contact materials¹

EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF)^{2,3}

DbdOpenFood

Apps The PubChem Project HOME Design Indaba GACS: GACS: substance Compendium of Bot Enterprise CompTox Dashboard SEURAT-1 - Towards https://dwh.efsa.eu

FILE VIEW FORMAT

Substance Characterisation						
Substance	has	Component	CAS Number	EC Ref No	Molecular formula	smiles
Ethylene glycol dipalmitate	as such	Ethylene glycol dipalmitate	624-03-3	210-826-5	C34H66O4	CCCCCCCCCCCCCCCC(=O)OCCOC(=O)CCCCCCCCCCCCCCCC

EFSA outputs							
	Id					Type	
Ethylene glycol dipalmitate	2621	Regulation (EC) No 1935/2004 (amended)	EFSA CEF	02/18/2015	Scientific Opinion on the safety assessment of the substance ethylene glycol dipalmitate, CAS No 624-03-3, for use in food contact materials	EFSA opinion	doi:10.2903/j.efsa.2015.4019

Hazard Characterisation: Reference points				
 No data returned for this view. This might be because the applied filter excludes all data.				

Hazard Characterisation: Reference values				
 No data returned for this view. This might be because the applied filter excludes all data.				

Genotoxicity				
Substance	Author	Year	Output Id	Genotoxicity
Ethylene glycol dipalmitate	EFSA CEF	2015	2621	Negative

Substance Browser

(CEF)-2015-EFSA_J....pdf Show all

SCIENTIFIC OPINION

Toxicological evaluation of benzophenone¹

Scientific Opinion of the Panel on food contact materials, enzymes, flavourings and processing aids (CEF)

DbdOpenFoodTOx. Micro

Secure | <https://dwh.efsa.europa.eu/bi/asp/Main.aspx?src=Main.aspx.2048001&evt=2048001&share=1&hiddensections=header%2Cpath%2CdockTop%2Cerror%2Che>

Apps The PubChem Project HOME Design Indaba | a bet GACS: GACS: substan Compendium of Bots Enterprise CompTox Dashboard SEURAT-1 - Towards <https://dwh.efsa.europa.eu>

FILTER

Substance Browser

Sub Name (4352)

benzophenone

☐ 2,4,4-Trifluorobenzophenone

☐ 4-Methylbenzophenone

☒ Benzophenone

☐ Benzophenone and 4-Hydr...

Substance Characterisation														
Substance	has	Component	CAS Number	EC Ref No	Molecular formula	smiles								
Benzophenone	as such	Benzophenone	119-61-9	204-337-6	C13H10O	C1=CC=C(C(=C1)C(=O)C2=CC=CC=C2								
EFSA outputs														
Substance	Output Id	Legal Basis		Panel	Published	Title					Output Type	Doi		
Benzophenone	415	Regulation (EC) No ...		EFSA	03/04/2009	EFSA statement on the presence of 4-methylbenzophenone found in					EFSA	doi:10.2903/j.efsa.2009.243r		
Hazard Characterisation: Reference points														
Substance	Author	Year	Output ID	Study	Test Type	Species	Route	Duration (days)	Endpoint	qualifier	value	unit	Effect	Toxicity
Benzophenone	EFSA CEF	2009	415	Human health	reproduction toxicity	Rat	Not reported		LOAEL	=	6	mg/kg bw/day	histopathology non neoplastic	he
Benzophenone	EFSA CEF	2009	477	Human health	chronic	Rat	oral; feed	735	BMDL10	=	3.1	mg/kg bw/day	histopathology non neoplastic	ne
Hazard Characterisation: Reference values														
Substance	Author	Year	Output Id	Assessment		qualifier	value	unit	Population					
Benzophenone	EFSA AFC	2008	2287	TTC Cramer Class III		=	1.5	µg/kg bw/day	Consumers					
Benzophenone	EFSA CEF	2009	477	TDI		=	0.03	mg/kg bw/day	Consumers					
Genotoxicity														
Substance	Author	Year	Output Id	Genotoxicity										
Benzophenone	EFSA CEF	2009	415	Negative										
Benzophenone	EFSA CEF	2009	477	Negative										

OPENFOODTOX IN KNOWLEDGE JUNCTION



OpenFoodTox: EFSA's chemical hazards database

April 10, 2017

Dataset **Open Access**

Indexed in
OpenAIRE

Publication date:
April 10, 2017

DOI:
DOI [10.5281/zenodo.344883](https://doi.org/10.5281/zenodo.344883)

Keyword(s):
contaminants critical study data collection data model
ecological hazard feed additives food additives
food contact materials food manufacturing products
nutrient sources pesticides processing aids
safety assessment substance toxicology

Subject(s):
contaminants data collection
dietary nutrient sources feed additives
food additives food industry pesticides
processing aids substances toxicology

Related identifiers:
Referenced by:
10.2903/sp.efsa.2013.EN-458,
10.2903/sp.efsa.2014.EN-654,
10.2903/j.efsa.2017.e15011

Communities:
Knowledge Junction

License (for files):
Creative Commons Attribution 4.0

Format: Excel (XLSX); Contact: data.collection@efsa.europa.eu

Name	Size	Download
EFSAOutputs_KJ.xlsx md5:5ce7a17f52c7872a15ce2da50c11533a	215.3 kB	Download
Genotoxicity_KJ.xlsx md5:5fdb8b7b884e30d0bc654445938f4e46e	97.2 kB	Download

Files (10.4 MB)

Full Download Knowledge junction:
https://zenodo.org/record/344883#.WUDqK_mGPIU

***Open Source in silico* Tools to Quantify Toxicological Processes**



-OPENFOODTOX AND *IN SILICO* TOOLS-

- 
- **Case studies** to develop *in silico* tools
 - **QSAR model on pesticide Toxicity in bees**
(OpenFoodTox, US-EPA, DEMETRA DB) : Classifier
 - **QSAR model to predict LC₅₀ in rainbow trout**
(OpenFoodTox) : Continuous model
 - Physico-chem properties, structure, toxicity : $R^2 > 0.75$
 - **QSAR model to predict NOAEL in rats** (OpenFoodTox, Fraunhofer) : Continuous model
 - Physico-chem properties, structure, toxicity : $R^2 > 0.75$
 - Scientific report Summer 2017



Contents lists available at ScienceDirect

Food and Chemical Toxicology

journal homepage: www.elsevier.com



The application of new HARD-descriptor available from the CORAL software to building up NOAEL models

Alla P. Toropova^{a,*}, Andrey A. Toropov^a, Marco Marzo^a, Sylvia E. Escher^b, Jean Lou Dorne^c, Nikolaos Georgiadis^c, Emilio Benfenati^a

^a Department of Environmental Health Science, Laboratory of Environmental Chemistry and Toxicology, IRCCS-Istituto di Ricerche Farmacologiche Mario Negri, Via La Masa 19, 20156 Milano, Italy

^b Fraunhofer Institute for Toxicology and Experimental Medicine ITEM, Hannover, Germany

^c Scientific Committee and Emerging Risks Unit, European Food Safety Authority, Via Carlo Magno 1A, 43126 Parma, Italy

ARTICLE INFO

Article history:

Received 11 November 2016

Received in revised form 16 March 2017

Accepted 28 March 2017

Available online xxx

Keywords:

QSAR

NOAEL

OECD principles

Monte Carlo method

CORAL software

ABSTRACT

Continuous QSAR models have been developed and validated for the prediction of no-observed-adverse-effect (NOAEL) in rats, using training and test sets from the Fraunhofer RepDose® database and EFSA's Chemical Hazards Database: OpenFoodTox. This paper demonstrates that the HARD index, as an integrated attribute of SMILES, improves the prediction power of NOAEL values using the continuous QSAR models and Monte Carlo simulations. The HARD-index is a line of eleven symbols, which represents the presence, or absence of eight chemical elements (nitrogen, oxygen, sulfur, phosphorus, fluorine, chlorine, bromine, and iodine) and different kinds of chemical bonds (double bond, triple bond, and stereo chemical bond). Optimal molecular descriptors calculated with the Monte Carlo technique (maximization of correlation coefficient between the descriptor and endpoint) give satisfactory predictive models for NOAEL. Optimal molecular descriptors calculated in this way with the Monte Carlo technique (maximization of correlation coefficient between the descriptor and endpoint) give amongst the best results available in the literature. The models are built up in accordance with OECD principles.



Our Vision

Our Mission

News & Updates

June, 2016
Working on behalf of UBA [The Platform for prioritising possible persistent, bioaccumulative and toxic \(PBT\) chemicals relies on VEGA](#)

June, 2016

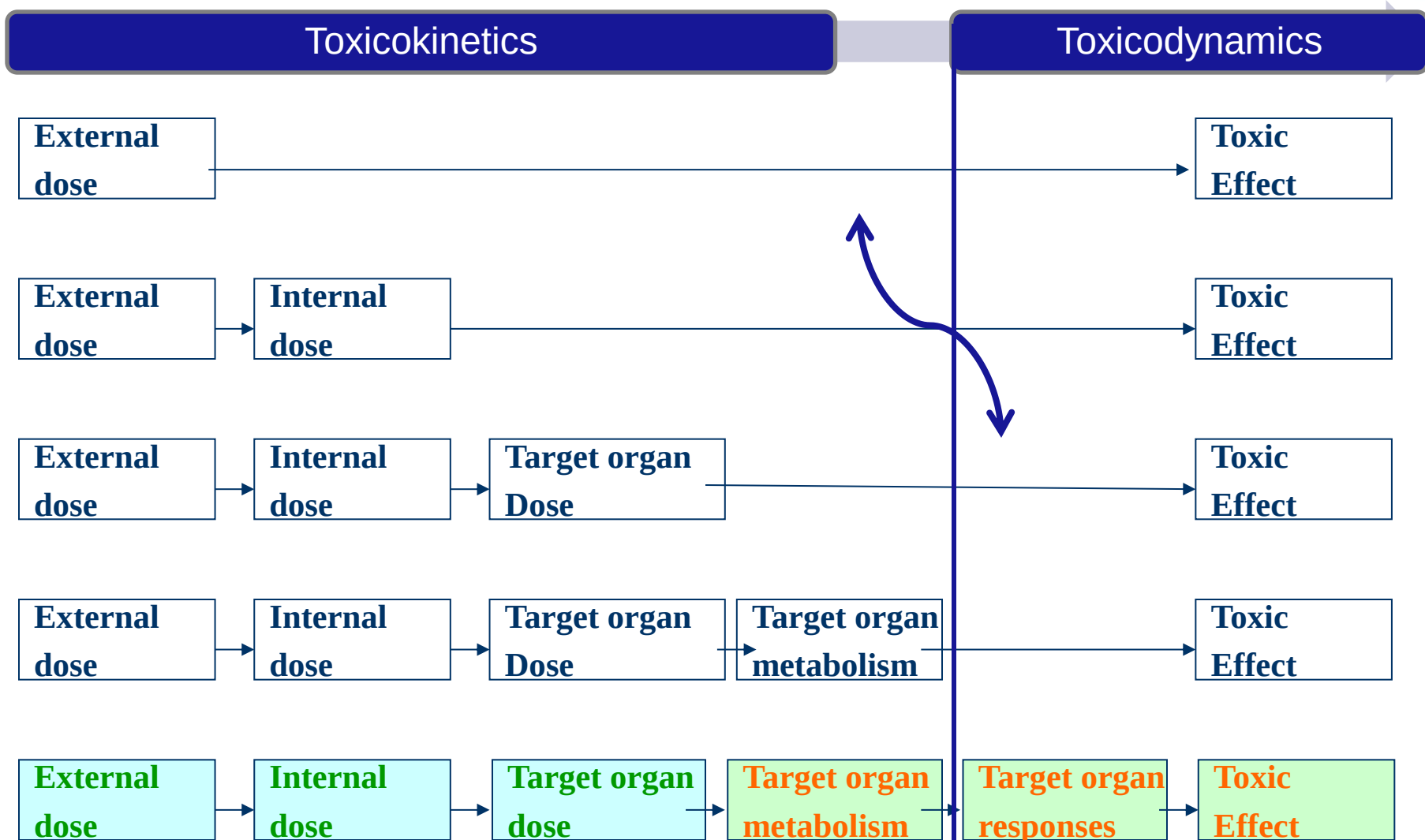
Our Community

On site

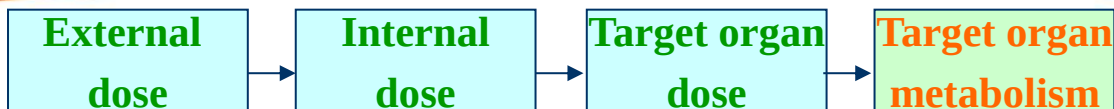
June, 2016
[How to interpret VEGA n explanation on how to has been added](#)

June, 2016
An example on how to u

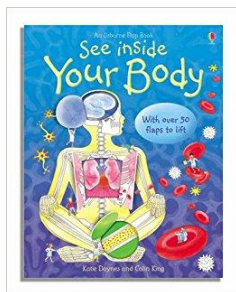
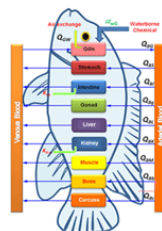
-Levels of Knowledge, Toxicokinetic and Toxicodynamic processes



TK PLATE: Physiology, Metabolism and Internal dose

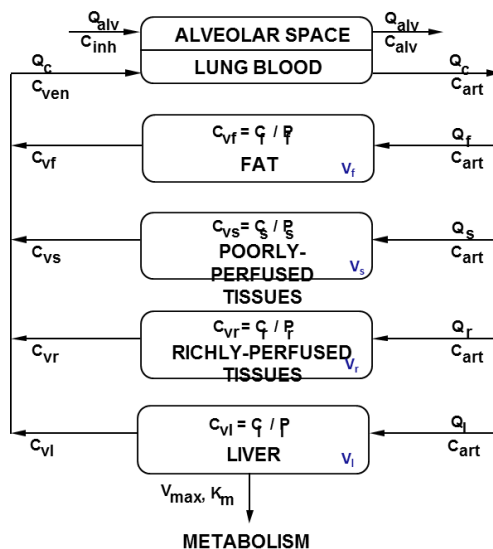


Physiological
Data



Metabolism
Data

Chemical-
Specific Data



Internal Dose
 TK parameters
 Tissue residues
 Interspecies Differences
 Human Variability



14 November
2016

🔗 Methodology

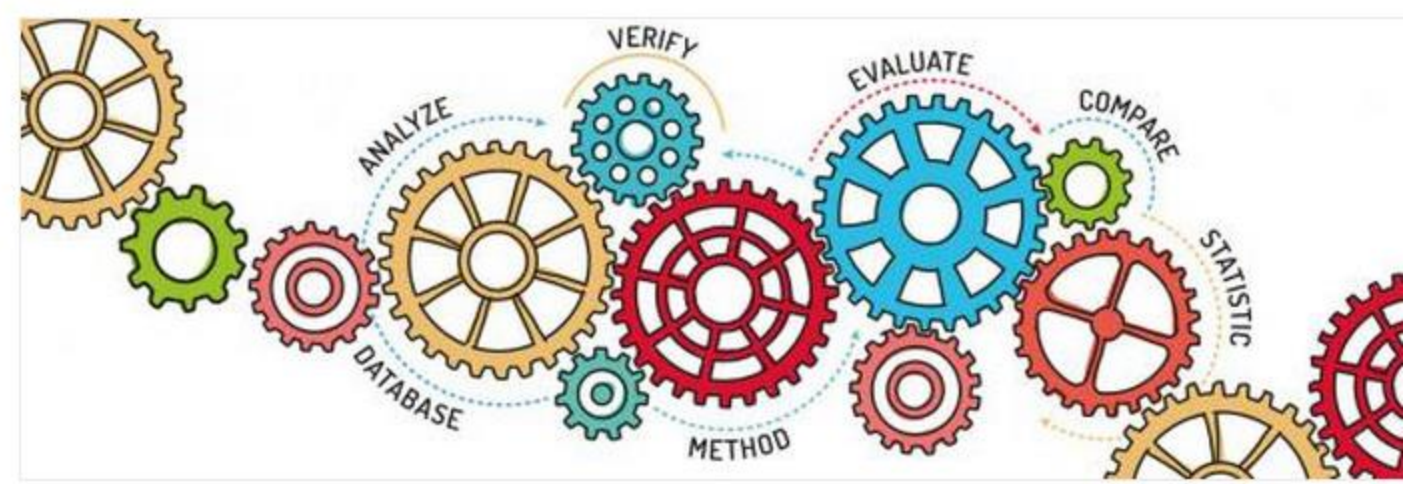
🖨️ print

🐦 Tweet

🌐 Share

📘 Share

Knowledge Junction – open access to scientific models



Scientific models used by EFSA over the last 15 years have been brought together in a new EFSA community: the **Knowledge Junction**. The models can be shared and cited and you can submit your own. A selection of these tools are also available as web applications on the new EFSA Statistical Models Platform; just

CONCLUSIONS AND RECOMMENDATIONS

- 
- ✓ **OpenFoodTox** provide **historical data** from EFSA RA Human, animal health and Ecological RA
 - ✓ **QSAR models** to support 3Rs and provide new tools
 - ✓ **Next for OpenFoodTox:**
 - Keep publishing Opensource data once/twice a year
 - Improve DB include physico-chemical properties/TK data
 - ✓ **Open Source TK models** to integrate exposure (external) to TK (internal) and Toxicity **by 2018**

ACKNOWLEDGEMENTS

- 
- ✓ **OpenFoodTox:** S-IN : Vicenza, Italy
 - ✓ **QSAR models :** Istituto Mario Negri, Milan, Italy
 - ✓ **TK platform:**
 1. Laser Analytica, Paris, France
 2. INERIS, Paris, France
 3. Radboud University, Nijmegen, The Netherlands
 - ✓ **TK/TD platform:**
 1. ANSES, Paris, France
 2. ISS, Rome, Italy
 3. University of Utrecht, Utrecht The Netherlands
 4. University of Bretagne, Brest, France

STAY CONNECTED!



Subscribe to

www.efsa.europa.eu/en/news/newsletters

www.efsa.europa.eu/en/rss



Engage with careers

www.efsa.europa.eu/en/engage/careers



Follow us on Twitter

[@efsa_eu](https://twitter.com/efsa_eu)

[@plants_efsa](https://twitter.com/plants_efsa)

[@methods_efsa](https://twitter.com/methods_efsa)

Many Thanks

Questions ?

jean-lou.dorne@efsa.europa.eu

