tds▶exposure

# TDS Exposure Assessment Tool MCRA

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This project has received funding from the European Union's Seventh Framework Programme
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# CONTENT

- What is the Monte Carlo Risk Assessment (MCRA) software
  - Support of Dutch Government, EFSA (pesticides), DG SANTE (pesticides)
- TDS exposure assessment achievements
  - harmonisation in Europe
  - how well are sources of variation and uncertainty covered
- How the MCRA modelling approach and TDS data can improve European risk assessment and risk management decisions
  - Methyl mercury
  - Acrylamide

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# MONTE CARLO RISK ASSESSMENT (MCRA)

Easy to use web-based software (mcra.rivm.nl)

## MCRA 8

MCRA stands for **Monte Carlo Risk Assessment**.
MCRA is a web-based system for probabilistic exposure and risk assessment of chemicals in the diet.
The MCRA system brings together statistical models, shared data and data uploaded by the user.
MCRA 8 also provides **Cumulative Exposure Assessment** for chemicals grouped in a Cumulative Assessment Group for which a single health effect is considered relevant.
Optionally exposure from other routes can be added in an **Aggregate Exposure Assessment**.
MCRA 8.0 was developed in EU project ACROPOLIS

Publications and reports using MCRA

### Login

Username

Password

Go to registration

LOGIN

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# Organize your data for MCRA

Introduction | User Manual | Data Formats Manual | Reference Documents | About | Contact

## Data formats manual

Download PDF
Download Template MDB

## Introduction

This Data Formats Manual is intended to assist with setting up the database files/spreadsheets for MCRA 8. File- or spreadsheet-names are restricted to maximum 50 characters length.

- Supported versions of MS Access are: Access 2000, Access 2003-2007 (extension '.mdb'), Access 2007-2010 (extension '.mdb' or '.accdb').
- Supported versions of MS Excel are: Excel 2010 (extension '.xlsx') and earlier versions (extension '.xls').

## General structure of the input data

The input databases/spreadsheets should provide sufficient information to run assessments. The input data (or assessment data) can be categorized into the following logical entity groups:

**Base entities:**

- Food data
- Compound data

**Assessment data:**

- Consumption data (data from a food survey)
- Concentration data (sample data)

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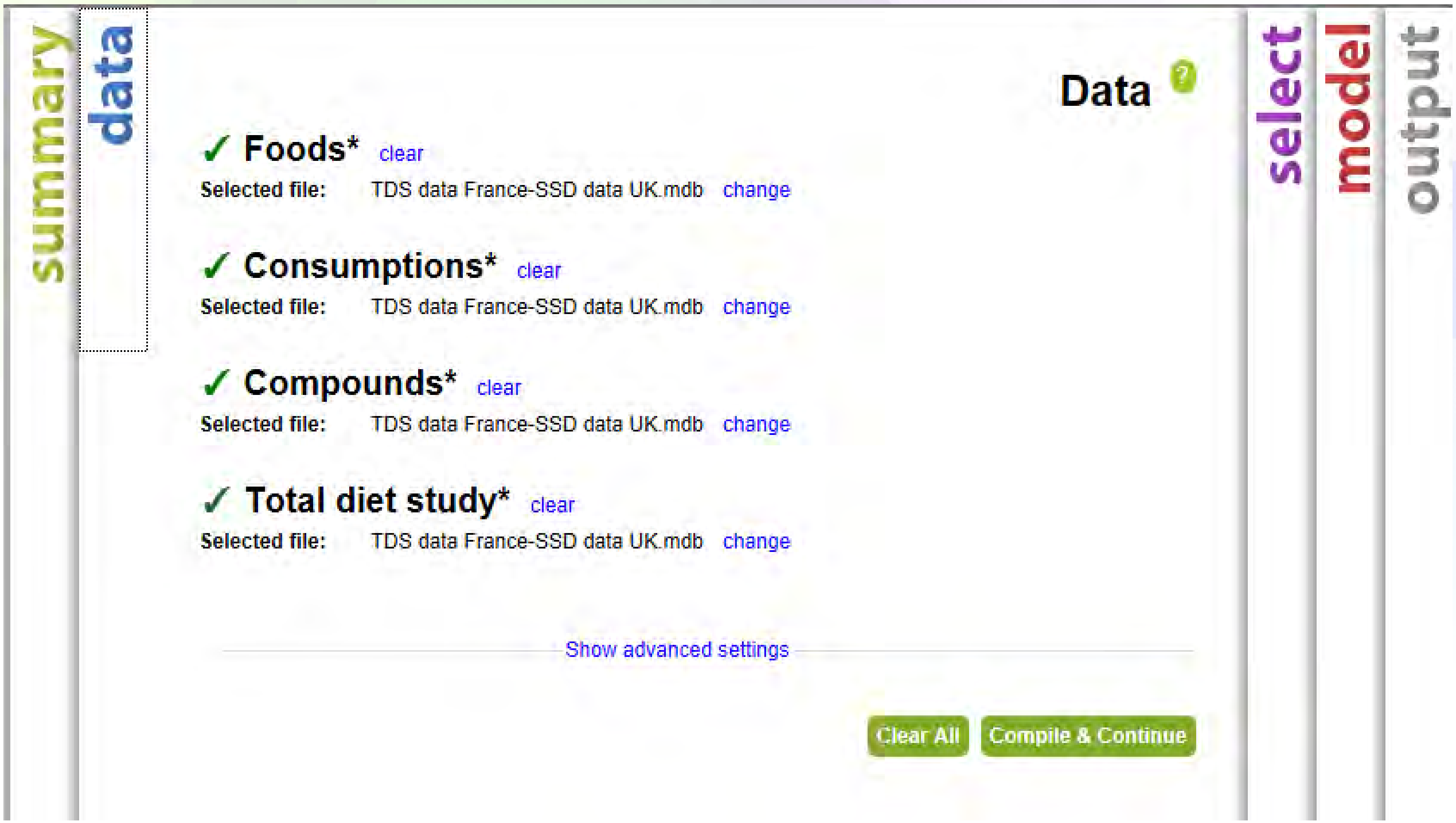
# Connect your data to MCRA

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# RELEVANT QUESTIONS FOR RISK ASSESSMENT

## DO WE OVER- OR UNDERESTIMATE

- Harmonization and exposure levels influenced by
  - harmonized food coding in Europe (FoodEx)
  - applying a usual intake model
- How representative is a TDS
  - seasonal and annual variation (e.g. DON)
  - regional variation (e.g. environmental contaminants)
  - variation in cooking and preparation methods (e.g. acrylamide)
- How complete is risk assessment based on TDS and/or monitoring

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# TRANSFORMATION OF TDS DATA TO EU-LEVEL

- Foodex coding, FoodCase-Risk, SSD format
- Historical TDS of the past and new TDS data in WP9

**Table 4: Percentiles of long-term exposure to dioxin-like compounds in adults living in Belgium, Netherlands, France, UK and Spain obtained via two classification systems**

| | Total dioxin-like compounds | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Exposure (pg TEQ/kg bw/day) | | | | | | | |
| | Using national codes | | | | Using FoodEx1 codes | | | |
| | P50 | P90 | P95 | P99 | P50 | P90 | P95 | P99 |
| Belgium | 0.69 | 1.46 | 1.82 | 2.60 | 0.65 | 1.40 | 1.75 | 2.61 |
| France | 0.39 | 0.78 | 0.95 | 1.38 | 0.40 | 0.76 | 0.91 | 1.21 |
| The Netherlands | 0.78 | 1.65 | 2.53 | 4.87 | 0.77 | 1.64 | 2.48 | 4.86 |
| Spain | 0.48 | 1.17 | 1.53 | 2.40 | 0.49 | 1.19 | 1.53 | 2.42 |
| UK | 0.99 | 1.55 | 1.76 | 2.23 | 0.99 | 1.55 | 1.75 | 2.16 |

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# How to address variation and uncertainty

- TDS is based on a sampling design
  - Variation might be well-covered or not covered in sampling design
  - 90-95% food items included in shopping list
  - Only pooled samples are analysed and consequently one measurement value for a pooled sample (variation lost)
- Monitoring data
  - Much more data available (variation known)
  - Only a limited number of food items monitored (incomplete)
  - Quite often biased towards problems (depends on sampling requirements in EU legislation)
- New exposure model based on mean (TDS) and variation (monitoring) implemented in the MCRA software

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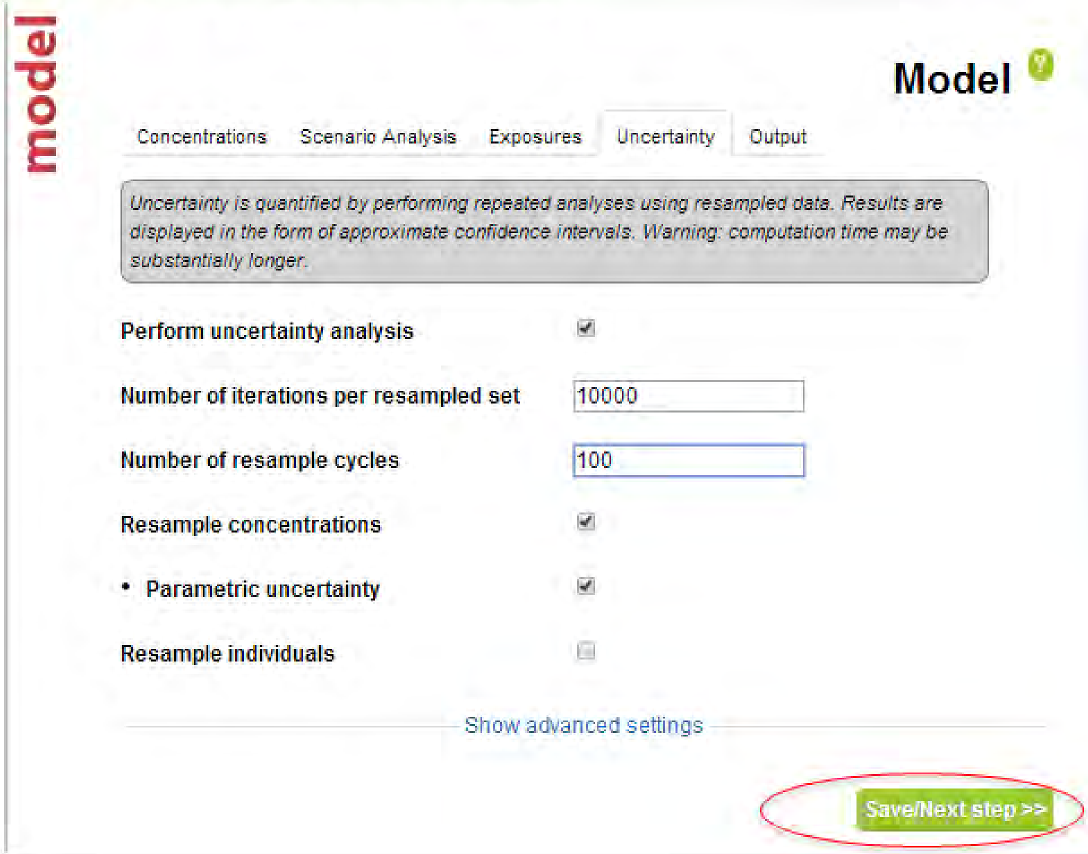
# How to address variation and uncertainty

## Model selection




1. Run with uncertainty
2. Include enough iteration to get a stable confidence interval (e.g use 100 resample cycles)
3. Use parametric uncertainty
4. Save/Next step

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# What if the variation in a TDS is not covered (example DON)

short
detailed
conversion

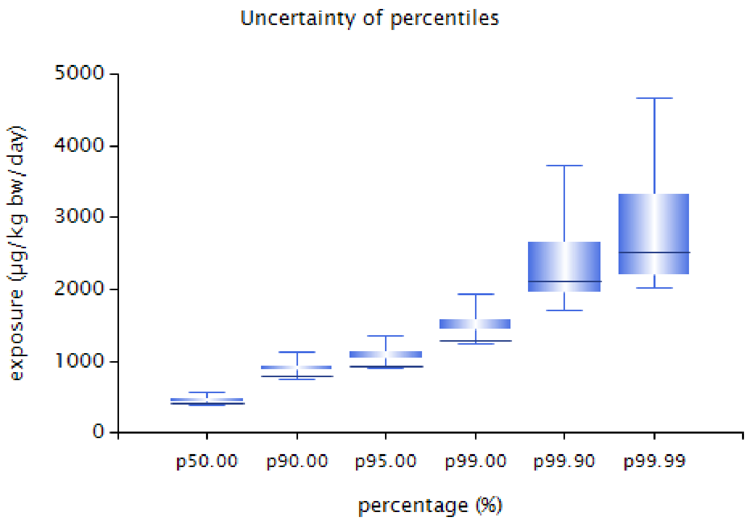
26-1-2015
14:4:3

DON variation TDS data France
CV = 2 (assumed)

## Exposure percentiles

TDI = 1000, upper bound 95% > TDI

| Percentage | Exposure (µg/kg bw/day) | Lower Bound (p2.5) | Upper Bound (p97.5) |
|---|---|---|---|
| 50.00 % | 417.2 | 391.2 | 573.6 |
| 90.00 % | 789.4 | 756.3 | 1130 |
| 95.00 % | 929.1 | 896.8 | 1341 |
| 99.00 % | 1292 | 1235 | 1938 |
| 99.90 % | 2114 | 1712 | 3715 |
| 99.99 % | 2509 | 2025 | 4659 |




1. If TDS is covering all sources of variation for DON, then the mean exposure can be trusted (no problem at the P95 for risk managers)
2. If TDS is not covering sources of variation for DON, you might wish to include additional information on variation as an uncertainty ( > TDI in red circle)

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# MCRA as a risk management tool, two case studies:

1) Acrylamide

2) Mercury and methylmercury in food


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# MCRA risk management tool case study acrylamide

- **Objective of this work**:
  - Test this risk management tool for acrylamide (AA) case study using a national TDS and monitoring data.
  - Show how expert opinion can be taken into account, and how a risk mitigation can be performed by setting limit values.
- **Data and Method:**
  - To assess the impact of a new regulation ('indicative values') on EFSA distribution of AA levels across food groups (EFSA, 2015)
  - To apply this impact on French TDS concentration data
  - To assess the impact on exposure and contributions

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# Occurrence data of AA per food category

**Table 5:** Distribution of acrylamide (AA) (middle bound (MB) estimates) according to the origin of data, expressed in µg/kg

| | Food category[h] | Origin[a] | n[b] | LC[c] | Mean[d] | Median[d] | P95[d] |
|---|---|---|---|---|---|---|---|
| 1 | **Potato fried products (except potato crisps and snacks)** | **EC** | 1 378 | 13.9 | 332 | 196 | 1 115 |
| | | **FA** | 316 | 15.8 | 201 | 170 | 493 |
| | French fries and potato fried, fresh or pre-cooked | | | | | | |
| 1.1 | / sold as ready-to-eat | EC | 877 | 12.7 | 308 | 218 | 904 |
| 1.2 | / sold as fresh or pre-cooked, analysed as sold | EC | 74 | 40.5 | 367 | 88 | 1 888 |
| 1.3 | / sold as fresh or pre-cooked, prepared as consumed[e] | EC | 241 | 14.5 | 288 | 103 | 1 059 |
| | | FA | 316 | 15.8 | 201 | 170 | 493 |
| 1.4 | / sold as fresh or pre-cooked, preparation unspecified | EC | 90 | 15.6 | 368 | 174 | 1 468 |
| 1.5 | Other potato fried products | EC | 96 | 2.1 | 606 | 544 | 1 549 |
| 2 | **Potato crisps and snacks** | **EC** | 800 | 7.0 | 580 | 389 | 1 841 |
| | | **FA** | 33 701 | 0.0 | 384 | 310 | 920 |
| 2.1 | Potato crisps made from fresh potatoes | EC | 498 | 6.6 | 654 | 431 | 2 050 |
| | | FA | 30 969 | 0.0 | 388 | 310 | 934 |
| 2.2 | Potato crisps made from potato dough | EC | 63 | 7.9 | 316 | 191 | 870 |
| | | FA | 2 732 | 0.3 | 338 | 298 | 747 |
| 2.3 | Potato crisps unspecified | EC | 216 | 7.9 | 519 | 348 | 1 465 |

Provided in the EFSA opinion on AA

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# EFSA opinion on indicative value for Acrylamide

**Table 2:** Indicative values for AA in foodstuffs according to Commission Recommendation 2013/647/EU

| **Foodstuff** | **Indicative value (µg/kg)** |
|---|---|
| French fries ready-to-eat | 600 |
| Potato crisps from fresh potatoes and from potato dough<br>Potato based crackers | 1 000 |
| Soft bread<br>- Wheat based bread<br>- Soft bread other than wheat based bread | <br>80<br>150 |
| Breakfast cereals (excl. porridge)<br>- bran products and whole grain cereals, gun puffed grain (gun puffed only relevant if labelled)<br>- wheat and rye based products[(1)]<br>- maize, oat, spelt, barley and rice based products[(1)] | <br><br>400<br>300<br>200 |

- Provided in the EFSA opinion on AA
- These values are not safety threshold but indicate the need to investigation

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# TDS Food correspondence with EFSA data

- Correspondence between TDS and EFSA food groups was established

| TDS food name | EFSA food group | Mean concentration | 95th percentile concentration | Indicative value (Limit) |
|---|---|---|---|---|
| Potato fried | Potato fried products (except potato crisps and snacks) | 332 | 1115 | 600 |
| Potato crisps | Potato crisps and snacks | 580 | 1841 | 1000 |
| Wheat bread and rolls | Wheat soft bread | 38 | 120 | 80 |
| Wheat bread, white | Wheat soft bread | 38 | 120 | 80 |
| Wheat bread, brown | Wheat soft bread | 38 | 120 | 80 |
| Wheat bread, with bran | Wheat soft bread | 38 | 120 | 80 |
| Wheat toast bread, white | Wheat soft bread | 38 | 120 | 80 |
| Corn flakes | Maize, oat, spelt, barley and rice based products | 73 | 230 | 200 |
| Cereal flakes | Breakfast cereals, unspecified | 100 | 350 | 200 |
| Muesli | Breakfast cereals, unspecified | 100 | 350 | 200 |
| Biscuits, sweet, plain | Biscuits and wafers | 201 | 810 | 500 |
| Biscuits, chocolate filling | Biscuits and wafers | 201 | 810 | 500 |
| Biscuits, fruit filling | Biscuits and wafers | 201 | 810 | 500 |
| Coffee drink, espresso | Roasted coffee (dry) | 244 | 563 | 450 |
| Instant coffee, liquid | Instant coffee (dry) | 674 | 1133 | 900 |

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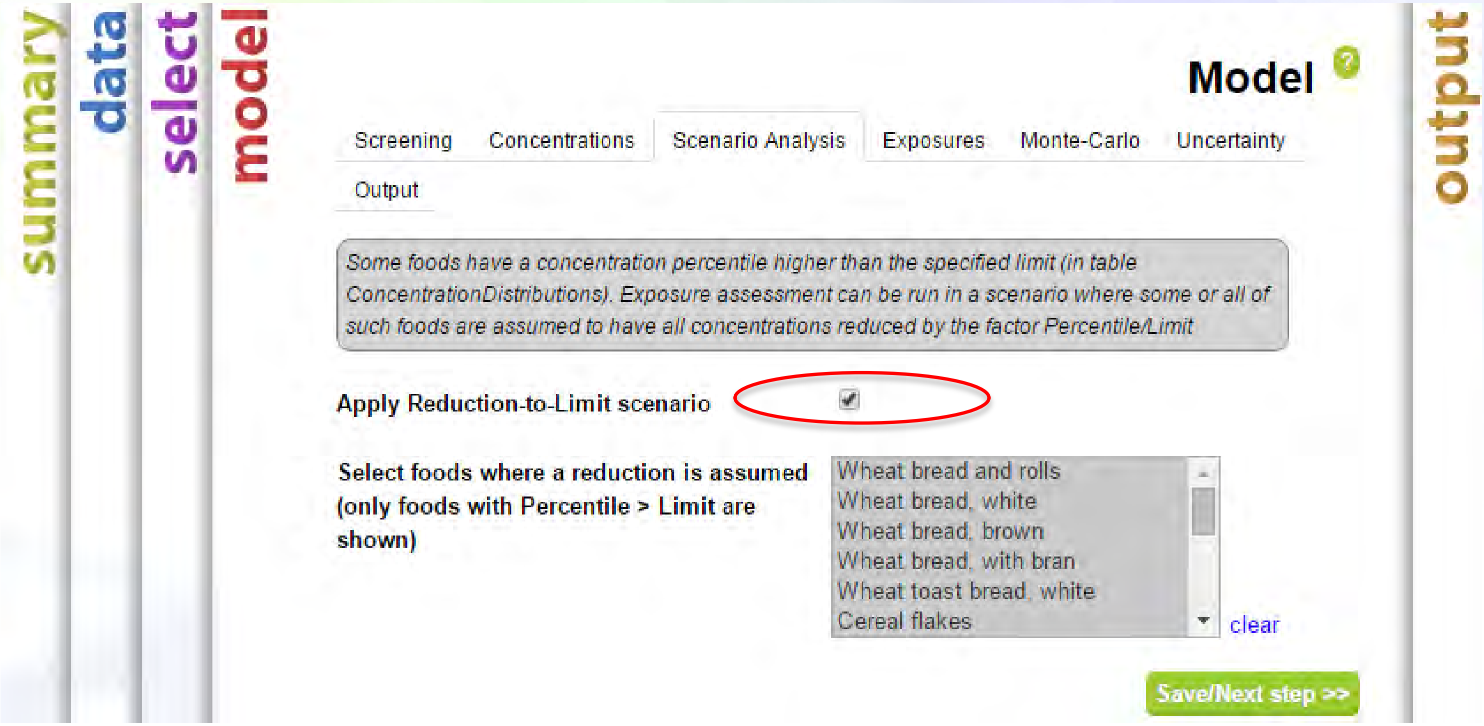
# How to perform analyses in MCRA

- **Model step:** to perform a reduction scenario select this option and foods
- Foods with a concentration higher than 'indicative value' are removed in exposure assessment

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# Results for AA case study: Exposure assessment

| Percentile | Without reduction scenario (ng/kg bw/day) | With reduction scenario (ng/kg bw/day) |
|---|---|---|
| 50 | 325.2 | 253.1 |
| 90 | 1371 | 843.2 |
| 95 | 1857 | 1144 |
| 99 | 3205 | 2053 |
| 99.90 | 4830 | 2802 |

Substantial reduction

Note: preliminary results. Results needs to be checked.

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# Results for AA study case: food contribution to total exposure

Without reduction scenario

| Food name | Contribution |
|---|---|
| Potato fried | 55.2 |
| Coffee drink, espresso | 12.2 |
| Biscuits chocolate filling | 6.63 |
| Snack food | 3.94 |
| Potato crisps | 3.30 |
| Pizza and pizza-like pies | 2.72 |
| Biscuits, sweet, plain | 1.51 |
| Wheat bread, white | 1.42 |
| Chocolate cake | 1.35 |
| Hot chocolate | 1.22 |
| Fruit pie | 0.96 |
| Wheat bread with bran | 0.95 |
| Chocolate (Cocoa) products | 0.88 |
| Instant coffee liquid | 0.87 |

With reduction scenario

| Food name | Contribution |
|---|---|
| Potato fried | 45.0 |
| Coffee drink, espresso | 14.8 |
| Biscuits chocolate filling | 6.20 |
| Snack food | 5.97 |
| Pizza and pizza-like pies | 4.12 |
| Potato crisps | 2.71 |
| Chocolate cake | 2.05 |
| Hot chocolate | 1.85 |
| Fruit pie | 1.45 |
| Wheat bread, white | 1.43 |
| Biscuits sweet plain | 1.41 |
| Chocolate (Cocoa) products | 1.34 |
| Cereal-based dishes | 1.19 |
| Instant coffee liquid | 1.04 |



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Note: preliminary results. Results needs to be checked.

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EC WORKING DOCUMENT, Expert Committee on Environmental and Industrial Contaminants (29/05/2015)

# Mercury and methylmercury in food

## Questions asked by the CZ food authority:

1. How new limits influence intake of Hg/MeHg for the whole CZ population?
2. What are the main Hg/MeHg risk drivers (foods) in CZ diet?
3. What limits we would need to keep at least 99,99% of population under EU HBDG?

   (= only 1000 persons will be over HBDG / CZ population 10M, = 10 pregnant women/year)

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# MCRA risk management tool methyl mercury

- **CZ TDS Data for years 2004-2013**
- **Expected concentrations of total mercury in foods** (mean + P95)
  - EFSA Journal 2012;10(12):2985: Scientific Opinion on the risk for public health related to the presence of mercury and methylmercury in food.
- **New limits for total mercury in foods**

  EC WORKING DOCUMENT, Expert Committee on Environmental and Industrial Contaminants (29/05/2015):Mercury and methylmercury in food

- **HBDG for risk characterization**
  - TWI for MeHg = 1,3 ug (expressed as Hg)/kg bw/w = 186 ng/kg bw/d (EFSA 2012)
  - TWI for inorganic Hg = 4 ug (expressed as Hg)/kg bw/w = 571 ng/kg bw/d (EFSA 2012)

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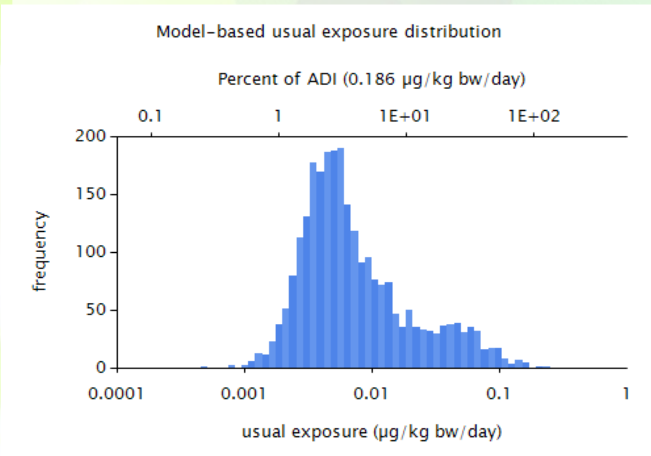
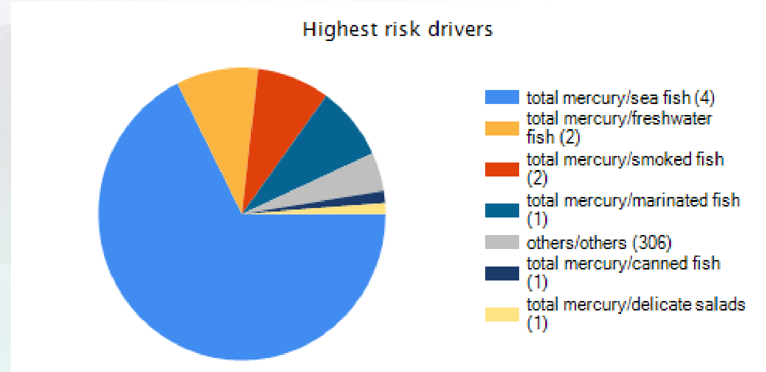
# MCRA test results: existing exposure UB




## Exposure percentiles

HBDG EFSA: Total mercury, **TDI = 0.186 (µg/kg bw/day),**
Mean exposure: 0.01375 (0.0132, 0.0144) (µg/kg bw/day)

TDI calculated from TWI for MeHg = 186 ng Hg/kg bw/d.
We used limit for MeHg because main risk drivers are linked with fish group where we expect at least 85% Hg in form of MeHg.

| Percentage | Exposure (µg/kg bw/day) | Lower bound (p2,5) | Upper bound (p97,5) | Percentage of reference dose |
|---|---|---|---|---|
| 50.00 | 0.005777 | 0.005675 | 0.005949 | 3.11 |
| 90.00 | 0.03709 | 0.03506 | 0.04033 | 19.94 |
| 95.00 | 0.05896 | 0.05568 | 0.06226 | 31.70 |
| 99.00 | 0.1008 | 0.0979 | 0.1119 | 54.20 |
| 99.90 | 0.1617 | 0.1506 | 0.1773 | 86.91 |
| 99.99 | 0.2365 | 0.1595 | 0.2413 | 127.15 |

Note: preliminary results. Results needs to be checked.

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# MCRA test results: when we apply new MLs - UB

## Exposure percentiles

HBDG EFSA: Total mercury, **TDI = 0.186 (µg/kg bw/day),**
Mean exposure: 0.01333 (0.01278, 0.014) (µg/kg bw/day)

| Percentage | Exposure (µg/kg bw/day) | Lower bound (p2,5) | Upper bound (p97,5) | Percentage of reference dose |
|---|---|---|---|---|
| 50.00 | 0.005629 | 0.005539 | 0.005829 | 3.03 |
| 90.00 | 0.03558 | 0.03244 | 0.03826 | 19.13 |
| 95.00 | 0.05725 | 0.05439 | 0.05949 | 30.78 |
| 99.00 | 0.1007 | 0.09714 | 0.1113 | 54.16 |
| 99.90 | 0.1616 | 0.1504 | 0.1763 | 86.89 |
| 99.99 | 0.2358 | 0.1594 | 0.2409 | 126.78 |

Practically no change in exposure doses for 99.9-99.99P.

**New MLs do not change intake of Hg considerably.**

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# MCRA test results: when we apply modified new MLs - UB

## + decrease limit for „sea fish“ to 0,3 mg/kg (instead of 0,5 mg/kg)

### Exposure percentiles

HBDG EFSA: Total mercury, **TDI = 0.186 (µg/kg bw/day),**
Mean exposure: 0.01011 (0.009624, 0.0107) (µg/kg bw/day)

| Percentage | Exposure (µg/kg bw/day) | Lower bound (p2,5) | Upper bound (p97,5) | Percentage of reference dose |
|---|---|---|---|---|
| 50.00 | 0.005629 | 0.005539 | 0.005829 | 3.03 |
| 90.00 | 0.03296 | 0.03046 | 0.03634 | 17.72 |
| 95.00 | 0.0524 | 0.04923 | 0.05617 | 28.17 |
| 99.00 | 0.09586 | 0.08822 | 0.101 | 51.54 |
| 99.90 | 0.1474 | 0.134 | 0.1597 | 79.25 |
| 99.99 | 0.2101 | 0.1462 | 0.2145 | 112.98 |

Note: preliminary results. Results needs to be checked.

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# CONCLUSIONS

(be aware of uncertainties related to data structure and character of usual TDS design; benefit of omega-3 FA not evaluated)

*1. How new limits influence intake of Hg/MeHg for the whole CZ population?*

- **New MLs do not change chronic intake of Hg/MeHg for CZ population (4-90y) considerably.**


*2. What are the main Hg/MeHg risk drivers (foods) in CZ diet?*

- **Sea fish foods are the main risk drivers for Hg/MeHg. Probability to be over MLs is about 5% (based on TDS data working with pooled samples).**

*3. What limits we would need to keep at least 99,99% of population under EU HBDG?*

- **Decreasing of ML for „sea fish“ on 0,3 mg Hg/kg foods (instead of 0,5 mg/kg) would protect about 99.99% of CZ population 4-90y. It does not take into account differences in sea fish species!)**
- **More than 99.99% of CZ women at child bear age (18-50y) is under HBDG even with old MLs.**

Note: preliminary results. Results needs to be checked.

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# Limitations of the approach

- Need to discuss the correspondence between food groups
  - Question of mixed dishes
  - Pooling foods from different groups? Ex: if we pooled snacks with potato crisps → different limits?

- A simple risk management model approach has been implemented, which should be improved based on better understanding of risk mitigation measures

- Result is a ‘proof of principle’

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# Validation of MCRA based on CZ biomonitoring data

- **Sampling of full blood:**
  - *Studied population groups*: **Adult men and women** (blood donors) aged **18 - 58 years**
  - About ***400 of blood samples per year*** (in total, 4472 adults from 1996 to 2009). Blood levels measured **annually** until 2003, since then **biannually**
  - The same **whole blood samples** for both biomarkers (Pb/Se)
- **Czech TDS ongoing since 1994**
  - Sampling period: until 2003 - 1 year, since 2004 - 2 years
- For comparison, we used two types of TDS results:
  - **Point estimate** (Tier 1 information) for average person (4-90 years).
  - **Monte Carlo Risk Assessment software** (MCRA), **Observed Individual Means** model (OIM) for specific age/sex groups and years

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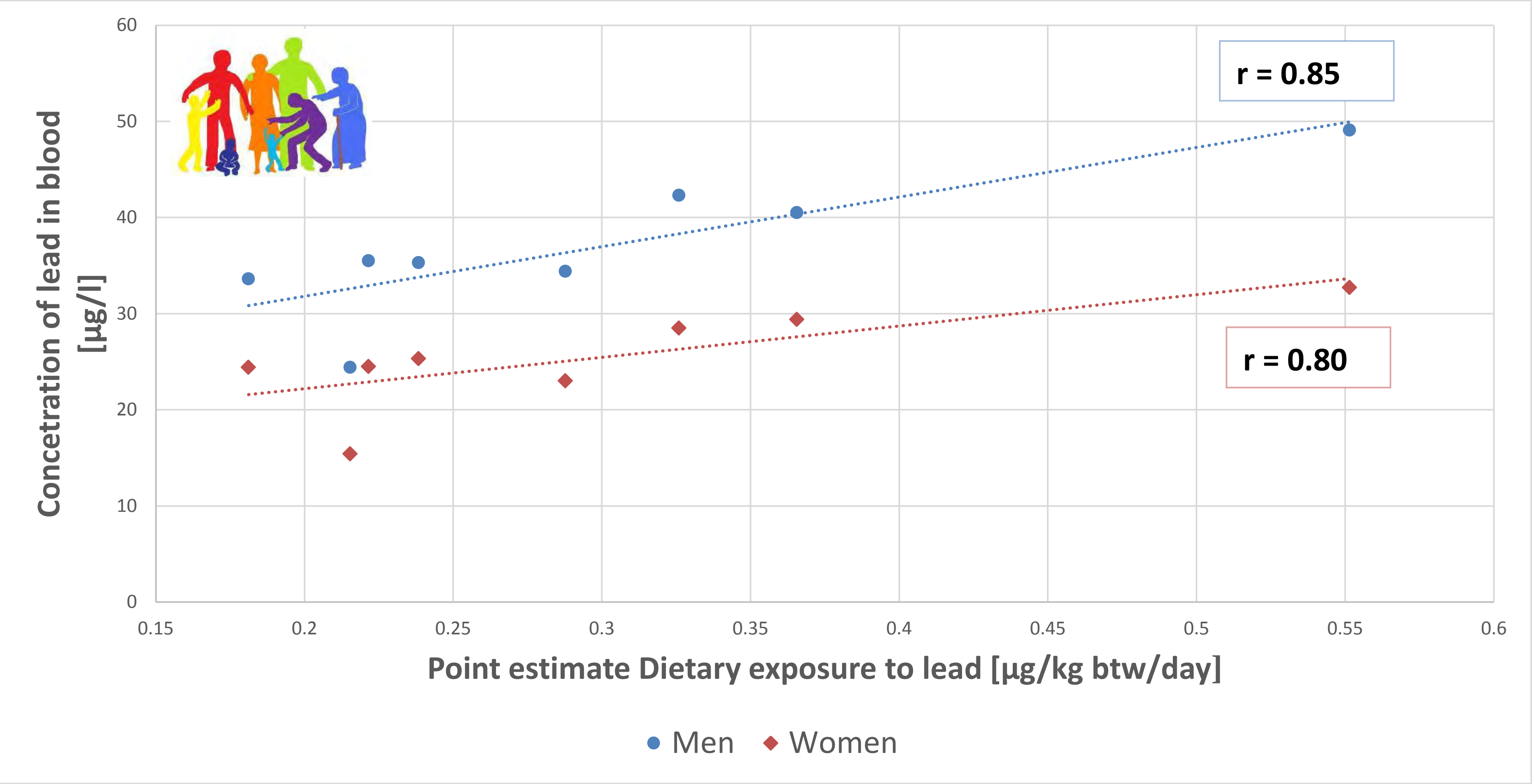
# Relationship between dietary exposure and blood lead levels
# Lead: TDS point estimate (average person aged 4 – 90 years)

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# Concluding remarks

- Exposure assessment using TDS data is harmonized at the European level using the MCRA software
- Variation and uncertainty are important and can affect the quality of the TDS exposure assessment results
- We demonstrated the relevance of using TDS data and the adjusted MCRA software for the European Commission in their discussion to set limits aiming to lower exposure levels
- TDS data should be used in future European risk assessment by EFSA and by European risk managers

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