Dietary exposure for risk assessment of GM foods

Ad hoc meeting with industry representatives

Parma, 24.10.2018
- Dietary exposure in the risk assessment of GM foods
- How to estimate dietary exposure
- Human dietary exposure: current situation
- Future
- Dietary exposure in the risk assessment of GM foods

- How to estimate dietary exposure

- Human dietary exposure: current situation

- Future
2. EXPOSURE ASSESSMENT — ANTICIPATED INTAKE/EXTENT OF USE

An estimate of the expected intake shall be an essential element in the risk assessment of genetically modified food and feed and shall also be required for the nutritional evaluation. Information shall be provided by the applicant on the intended function, the dietary role, and the expected level of use of the genetically modified food and feed in the EU. In addition, the expected range of concentrations of newly produced proteins or existing plant proteins deliberately modified in the genetically modified food(s) and feed(s) to be placed on the market shall be provided.

The applicant shall determine by appropriate methods the concentrations of the newly expressed proteins, other new constituents and endogenous food and feed constituents, of which the levels have been altered as a result of the genetic modification (for example, due to changes in metabolic pathways) in those parts of the genetically modified plant intended for food or feed use. Expected intake of these constituents shall be estimated taking into account the influences of processing, storage and expected treatment of the food and feed in question, for example, potential accumulation or reduction. In cases where the genetic modification has resulted in an altered level of a natural constituent, or if a new constituent occurs naturally in other food and feed products, the anticipated change in total intake of this constituent shall be assessed considering realistic as well as worst case intake scenarios.
**DIETARY EXPOSURE AS PART OF THE RA OF GM FOOD**

- **Comparative dietary exposure frame**: dietary exposure of similar/identical proteins in different foods & dietary exposure to NEPs.
  
  - e.g. XXXX protein in GM-crop & XXXX present in different conventional foods (oat, maize, wheat, rice, barley).

- **Absolute dietary exposure frame**: dietary exposure to NEPs & health based guidance values (risk characterization).
- Dietary exposure in the risk assessment of GM foods

- **How to estimate dietary exposure**

- Human dietary exposure: current situation

- Future
GMO DIETARY EXPOSURE ASSESSMENT

Field trials – DOSSIER -

Food Terminology
FOODEX

EFSA Comprehensive European food consumption database

Concentration values* → Dietary exposure (EXTERNAL) → Food consumption

Scenario 100% replacement
CONCENTRATION DATA

- Substances are analysed in raw primary commodities and consumption data refers to blended (processed) commodities.

- In most of the cases, very (very) small number of samples available....representative??

Which values should be used for dietary exposure estimations?

Chronic dietary exposure and acute dietary exposure
CONCENTRATION DATA

Which values to estimate dietary exposure to GMO components?

When using **NEP concentrations from RPC** the most realistic scenario is to always* use **MEAN CONCENTRATIONS** for both **ACUTE** and **CHRONIC EXPOSURE**
WHICH CONCENTRATION DATA TO BE USED (FROM THE RPC)

- Appropriate material at the representative growth stage (e.g. maize: grains R6/senescence)

- Representative of cultivation conditions (crops treated with the intended herbicide).

- Mean values (acute and chronic dietary exposure).
  *Possibility of differentiating among areas (sites) if significant differences reported

- Values expressed in fresh weight

- LOD/LOQ to be used for left-censored data (undetected/unquantified) when estimating mean values.
Factors and recipes linked to processed commodities are also considered.

- **Recipes** = dilution effect
- **Reverse yield factors**: conservative approach*
  - no NEP losses (e.g. due to fermentation)
  - No effect of processing (pH, temperature) as related to the potential hazard of the NEP

Protein content
- More accurate when covering processed commodities made of different foods.

- **On-going** work on recipes & factors (RPC model)

- Harmonised approach across EFSA
FROM RPC DATA TO PROCESSED COMMODITIES

Identify relevant commodities that may contain our compound of interest (e.g. NEP)

<table>
<thead>
<tr>
<th>Bread</th>
<th>Maize, popped</th>
<th>Popcorn</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corn flour</td>
<td>Corn syrup</td>
<td>Rosehip soup</td>
</tr>
<tr>
<td>Corn semolina</td>
<td>Corn oil</td>
<td>Blueberries soup</td>
</tr>
<tr>
<td>Corn starch</td>
<td>Whisky</td>
<td></td>
</tr>
<tr>
<td>Cornmeal</td>
<td>Gin</td>
<td></td>
</tr>
<tr>
<td>Corn flakes</td>
<td>Grain soup</td>
<td></td>
</tr>
</tbody>
</table>

- Sweet corn
- Prepared pasta salad
- Mashed vegetables
- Mixed vegetables fried, Mexican
- Mixed vegetables, grilled
- Mixed vegetables boiled, Mexican
- Prepared mixed vegetable salad

Maize grain

Sweet corn
(Zea mays var. saccharata)
From RPC data to processed commodities

Maize consumption

Mean value (n=15)
10 µg NEP/kg fresh weigh

Standard recipe for maize bread (Mintel database)
Maize flour (74%), sunflower oil (3%), tap water (20%), salt (2%) and yeast (1%)

Milling = 1.22

74 grams → 100 grams

122 grams

0.74 × 1.22

Factor\textsubscript{BREAD} = 0.92
## FROM RPC DATA TO PROCESSED COMMODITIES

<table>
<thead>
<tr>
<th>FOODEX LEVEL</th>
<th>FOODEX CODE</th>
<th>FOOD</th>
<th>Amount of raw agricultural commodity to produce 100 grams of processed food (grams)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>6220</td>
<td>Corn grain</td>
<td>100</td>
<td>100% grain</td>
</tr>
<tr>
<td>3</td>
<td>8074</td>
<td>Popcorn</td>
<td>100</td>
<td>Puffing=1,08, 92,9% grain</td>
</tr>
<tr>
<td>4</td>
<td>6268</td>
<td>Corn flour</td>
<td>122</td>
<td>Milling= 1,22, 100% Corn flour</td>
</tr>
<tr>
<td>4</td>
<td>6383</td>
<td>Corn flakes</td>
<td>260</td>
<td>100% Corn flakes</td>
</tr>
<tr>
<td>4</td>
<td>6384</td>
<td>Corn flakes and nuts</td>
<td>190</td>
<td>73% Corn flakes</td>
</tr>
<tr>
<td>4</td>
<td>6385</td>
<td>Corn flakes with honey and nuts</td>
<td>156</td>
<td>Flaking = 2,6, 60% Corn flakes</td>
</tr>
<tr>
<td>4</td>
<td>6386</td>
<td>Corn flakes with honey and sugar</td>
<td>190</td>
<td>73% Corn flakes</td>
</tr>
<tr>
<td>4</td>
<td>6387</td>
<td>Corn flakes with sugar</td>
<td>161</td>
<td>62% Corn flakes</td>
</tr>
<tr>
<td>4</td>
<td>6445</td>
<td>Cornmeal porridge</td>
<td>18</td>
<td>15% corn grain (cornmeal)</td>
</tr>
<tr>
<td>4</td>
<td>6271</td>
<td>Cornmeal</td>
<td>122</td>
<td>Milling= 1,22</td>
</tr>
<tr>
<td>4</td>
<td>6269</td>
<td>Corn semolina</td>
<td>122</td>
<td>Milling= 1,22</td>
</tr>
<tr>
<td>4</td>
<td>6352</td>
<td>Corn bread</td>
<td>91</td>
<td>Milling= 1,22, Corn flour 74,3%</td>
</tr>
<tr>
<td>3</td>
<td>6336</td>
<td>Multigrain bread and rolls</td>
<td>3</td>
<td>Milling= 1,22, Corn flour 2,4 %</td>
</tr>
<tr>
<td>3</td>
<td>6407</td>
<td>Muesli bars</td>
<td>26</td>
<td>Flaking = 2,6, 10% cornflakes</td>
</tr>
<tr>
<td>4</td>
<td>6422</td>
<td>Maize, popped</td>
<td>108</td>
<td>Puffing=1,08, 100% grain</td>
</tr>
<tr>
<td>4</td>
<td>6423</td>
<td>Maize, popped, with sugar</td>
<td>100</td>
<td>67% corn flour + 33% sugar</td>
</tr>
</tbody>
</table>
CONSUMPTION DATA

- Two main sources of consumption data used in the past in GM applications:
  - Pesticide Residues Intake MOdel (PriMo) model
  - FAO's Food Balance Sheets (FBSs)

- It allowed a direct link of the levels of particular constituents measured in RPCs with the consumption data of RPCs
CONSUMPTION DATA

- Some drawbacks associated to the use of PriMo model and/or FBS:
  - FBSs are not appropriate for acute exposure
  - Primo model
    - different methodology to disaggregate the consumption data
    - no possibility to exclude particular foods

**EFSA statement in 2015 on the use of the EFSA Comprehensive Consumption database in GMO area**
The EFSA Comprehensive European food consumption database contains data:

- 24-hour recall or dietary record method
- Data collected at individual level
- Most recent data within each country
- Random sample at national level
- Different age classes, from infants to elderly
- Special population groups
<table>
<thead>
<tr>
<th>Number of</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Member States</td>
<td>25</td>
</tr>
<tr>
<td>Dietary surveys</td>
<td>60</td>
</tr>
<tr>
<td>Population groups</td>
<td>132</td>
</tr>
<tr>
<td>Subjects</td>
<td>119,458</td>
</tr>
<tr>
<td>Consumption records</td>
<td>12,076,637</td>
</tr>
</tbody>
</table>

Last update in Aprile 2018
## EFSA COMPREHENSIVE CONSUMPTION DATABASE - AGE CLASSES -

<table>
<thead>
<tr>
<th>Age class</th>
<th>Age range (years)</th>
<th>Number of surveys*</th>
<th>Number of countries*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before April 2018</td>
<td>After April 2018</td>
<td>Before April 2018</td>
</tr>
<tr>
<td>Infants</td>
<td>0 – 1</td>
<td>6</td>
<td>11 (11)</td>
</tr>
<tr>
<td>Toddlers</td>
<td>1 – 3</td>
<td>11 (10)</td>
<td>15 (14)</td>
</tr>
<tr>
<td>Children</td>
<td>3 - 10</td>
<td>20 (18)</td>
<td>21 (19)</td>
</tr>
<tr>
<td>Adolescents</td>
<td>10 - 18</td>
<td>20 (17)</td>
<td>21 (18)</td>
</tr>
<tr>
<td>Adults</td>
<td>18 - 65</td>
<td>22 (17)</td>
<td>23 (19)</td>
</tr>
<tr>
<td>Elderly</td>
<td>65 - 75</td>
<td>16 (14)</td>
<td>20 (18)</td>
</tr>
<tr>
<td>Very elderly</td>
<td>&gt; 75</td>
<td>14 (12)</td>
<td>17 (15)</td>
</tr>
<tr>
<td>Special population group</td>
<td>2 (2)</td>
<td>4 (4)</td>
<td>2 (2)</td>
</tr>
</tbody>
</table>

* In parenthesis only surveys with more than one day per subject
- Chronic/acute dietary exposure

- Average population and high consumers

- Estimated in different age classes across Europe

- Special population groups: vegetarians, lactating women and pregnant women.
- Dietary exposure in the risk assessment of GM foods
- How to estimate dietary exposure
- Human dietary exposure: current situation
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CURRENT SITUATION

- Dietary exposure to NEP thoroughly addressed and reported in SO from AP-121 onwards.*

- Information reported in the SO: acute and chronic dietary exposure, only high consumers.

- Information provided by the applicants: very diverse
  - Inconsistency between scope and assessment; indistinct use of expression of results (fresh weight/dry weight); chronic exposure/acute dietary exposure not provided; missing information on high consumers; inadequate use of summary statistics on consumption...

- Preparation of a document providing guidance to harmonise data needed on exposure estimations.
Summary food consumption statistics (chronic and acute) available per

- country,
- survey,
- age group (from infants to elderly)
- codified in FoodEx
- in g/day and g/kg bw per day.

- Use of the most recent dietary surveys per country and age class
- Use of appropriate FoodEx levels
Chronic dietary exposure in the average population
Sum the exposure of all relevant foods obtained by multiplying the average consumption of each food in the whole population by the mean value reported in the GM crop for the compound of interest (e.g. NEP).

Chronic dietary exposure of high consumers
Sum the high percentile (e.g. 95th) of the most consumed food among consumers only and the average consumption of all the other foods in the whole population, using the mean value reported in the GM crop for the compound.

“Overview of the procedures currently used at EFSA for the assessment of dietary exposure to different chemical substances” (EFSA, 2011)
Food additives intake model (FAIM) Template (2012)
Acute dietary exposure for the average population and high consumers.

As we talk about acute exposure, the consumption refers to the amount of food commodity consumed in only one day so the summary statistics for acute consumption should be used. For the rest, same approach as for chronic exposure.
CONSUMPTION DATA

- Use of EFSA Comprehensive Consumption database (summary statistics) allows...
  - Assessment *chronic* and *acute* dietary exposure (screening tool)
  - *Average* and *high consumers*
  - *Extensive coverage* of European population
  - Selection of *food commodities relevant for exposure*
  - Possibility of looking at *vulnerable* population groups (based on age, consumption habits, life status)
- Dietary exposure in the risk assessment of GM foods
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**AIM:** To provide guidance on how human dietary exposure to GM constituents should be estimated making the best use of the available information. Description of the information needed for the RA (standardisation)

- Presentation based on the on-going document; your feedback is very welcome!
- Publication first quarter of 2019
Concentration data to be used (mean values, fresh weight, use LOD/LOQ, etc.)

How to best use summary statistics on consumption data

Recipes and factors provided in EFSA website

Information to be provided as part of the submission dossier
RAW PRIMARY COMMODITY MODEL (RPC MODEL)

Raw Primary Commodities (RPCs)

Food as consumed

Reverse yield factors

List of ingredients and proportions

Individual ingredients
GMO DIETARY EXPOSURE ASSESSMENT

Field trials – DOSSIER -

Food Terminology
FOODEX

EFSA Comprehensive European food database

Raw Primary Commodities
(RPC MODEL)

Concentration values*

Dietary exposure
(EXTERNAL)

Food consumption

Scenario 100% replacement
TAKE HOME MESSAGES ON DIETARY EXPOSURE

- Dietary exposure to be used on concluding on the safety of the endogenous/new constituents = representative and accurate levels needed!!

- Dietary exposure estimations today could be different tomorrow: need of monitoring different outcome of the RA still SAFE?
There are uncertainties surrounding dietary exposure estimations

Assumptions introduce uncertainty

Overall: conservative estimations

Realistic and representative

Where can the uncertainty be reduced?

- Consumption: 100% replacement 😞
- Improve representativity of samples ?? 😞
- Accuracy of the measurements?? 😊
- Appropriate use of the available data (mean, fresh weight, etc.) 😊
- Concentration data on processed foods ?? 😞
- Processing studies...at the moment only DILUTION due to recipes... 😞
THANKS!!

QUESTIONS?