Info session on applications for feed additives

Parma, 14 and 15 November 2019

Assessing consumer exposure to feed additives: from theory to practice

O. Holczknecht, MV. Vettori

FEED Unit

Trusted science for safe food

efsa
European Food Safety Authority

Data requirements for exposure assessment

Reg. (EC) No 429/2008 and Guidance on the assessment of the safety of feed additives for the consumer (EFSA FEEDAP Panel, 2017)

Technical dossier/Section III

- Residue data
  - Residues in tissues and products measured in a residue study
  - Alternatively: residues can be measured in a tolerance study

- Full toxicological dataset
  - Allowing the determination of:
    - A safe dose (e.g. NOAEL)
  - Allowing the establishment of:
    - A health-based guidance value (e.g. ADI)

Steps of consumer exposure assessment

Step 1: Calculation of exposure via FACE

- Input: Residue data
- Output: Exposure

Step 2: Comparison of the exposure with the health-based guidance value

FACE – Input: total residue data

Table 1. Total residue concentrations in tissues of chickens for fattening administered xx mg additive/kg feed

	Liver	Kidney	Muscle	Skin/fat
TRC + 2SD (mg/kg)	0.618	0.190	0.033	0.350

The residue concentration in muscle and skin/fat will be applied to the intake of meat at the following proportions: 90% muscle and 10% skin/fat. This corresponds to 0.065 mg/kg.

Raw Primary Commodity	Metrics	Occurrence level (mg/kg)
Birds fat tissue	A0F1E	0.35
Birds liver	A16YS	0.618
Birds meat	A0EYG	0.065
Birds offals and slaughtering products (other than liver)	A16YV	0.190
Fish (meat)	A026V	0.000000
Honey	A033J	0.000000
Mammals fat tissue	A0F3G	0.000000
Mammals liver	A0F3J	0.000000
Mammals meat	A0EYF	0.000000
Mammals offals and slaughtering products (other than liver)	A16YT	0.000000
Milk	A02LT	0.000000
Seafood	A16YX	0.000000
Whole eggs	A031F	0.000000

Submit

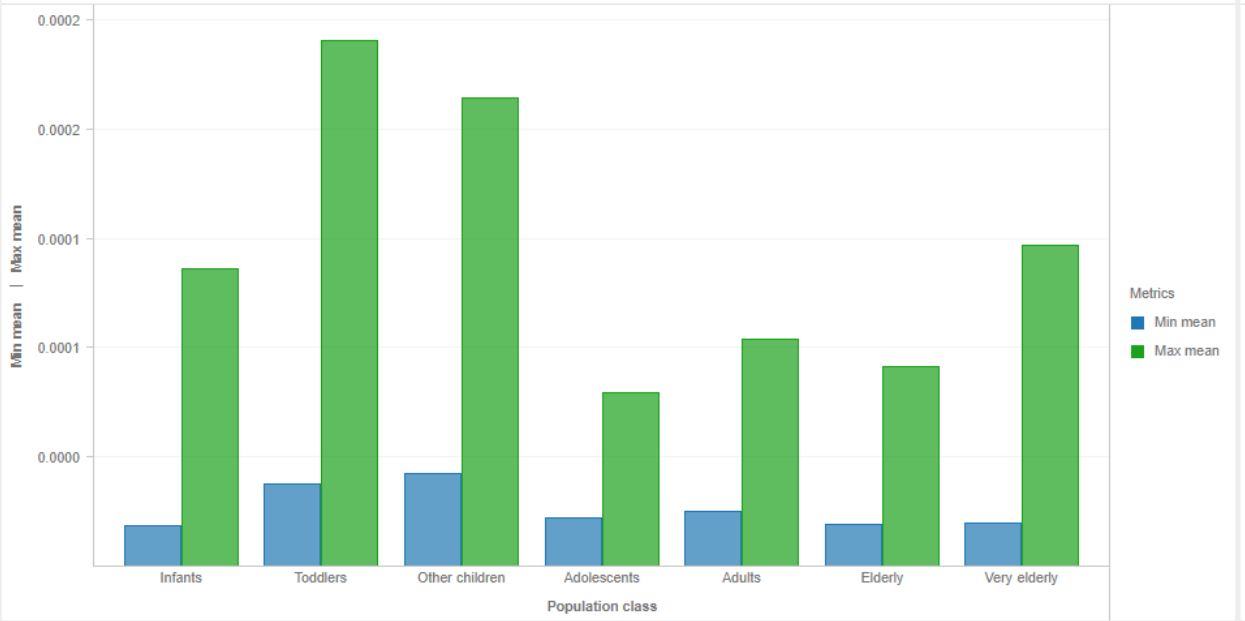
FACE – Output: exposure

FILE

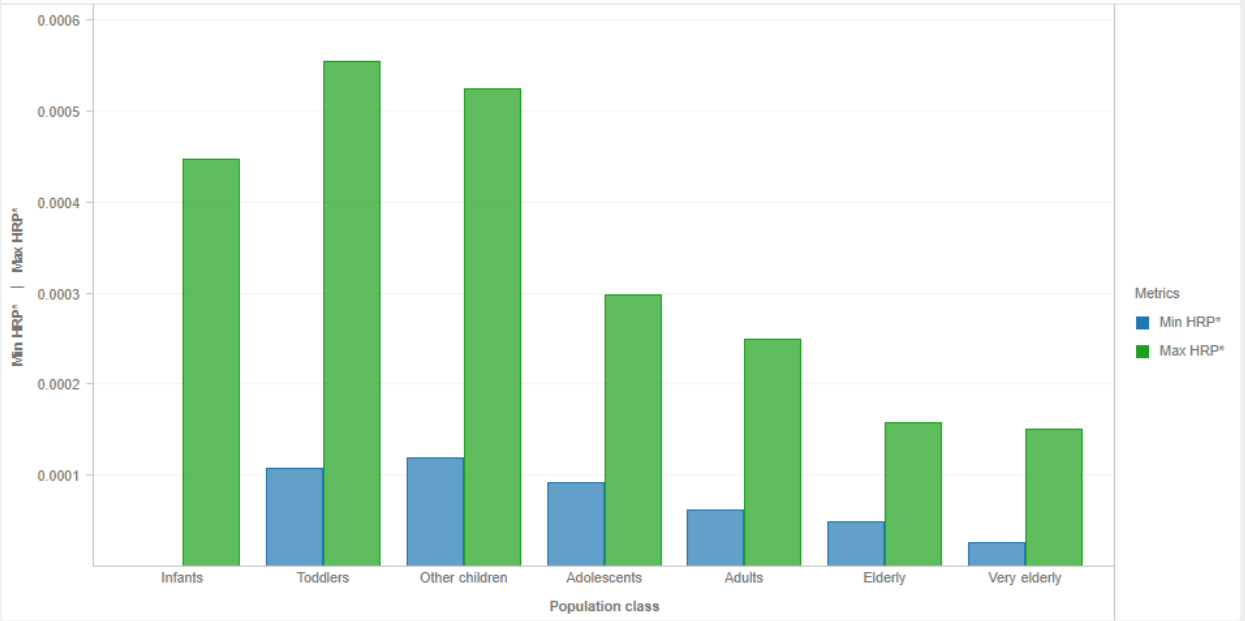
Summary statistics of the chronic dietary exposure assessments across European dietary surveys (mg/kg body weight per day)

Population class	Number of surveys	Minimum mean	Maximum mean	Minimum HRP*	Maximum HRP*
Infants	6	0.0000	0.0001	0.0000	0.0004
Toddlers	10	0.0000	0.0002	0.0001	0.0006
Other children	18	0.0000	0.0002	0.0001	0.0005
Adolescents	17	0.0000	0.0001	0.0001	0.0003
Adults	17	0.0000	0.0001	0.0001	0.0002
Elderly	14	0.0000	0.0001	0.0000	0.0002
Very elderly	12	0.0000	0.0001	0.0000	0.0002

Summary graph of the mean chronic dietary exposure (mg/kg body weight per day)



Summary graph of the HRP* chronic dietary exposure (mg/kg body weight per day)



* HRP: highest reliable percentile, i.e. the highest percentile that is considered statistically robust for combinations of dietary survey, age class and possibly raw primary commodity, considering that a minimum of 5, 12, 30 and 61 observations are respectively required to derive 50th, 75th, 90th and 95th percentile estimates. Estimates with less than 5 observations were not included in this table.

Chronic summary | Chronic mean graph | Chronic HRP graph | Chronic contributions | Chronic details | Acute summary | Acute details | Occurrence data

FACE – How to interpret the results

CHRONIC assessment

In case the health-based guidance value is derived from a toxicology study with a chronic endpoint.

vs

ACUTE assessment

In case the health-based guidance value is derived from a toxicology study with an acute endpoint.

FACE – How to interpret the results - Chronic

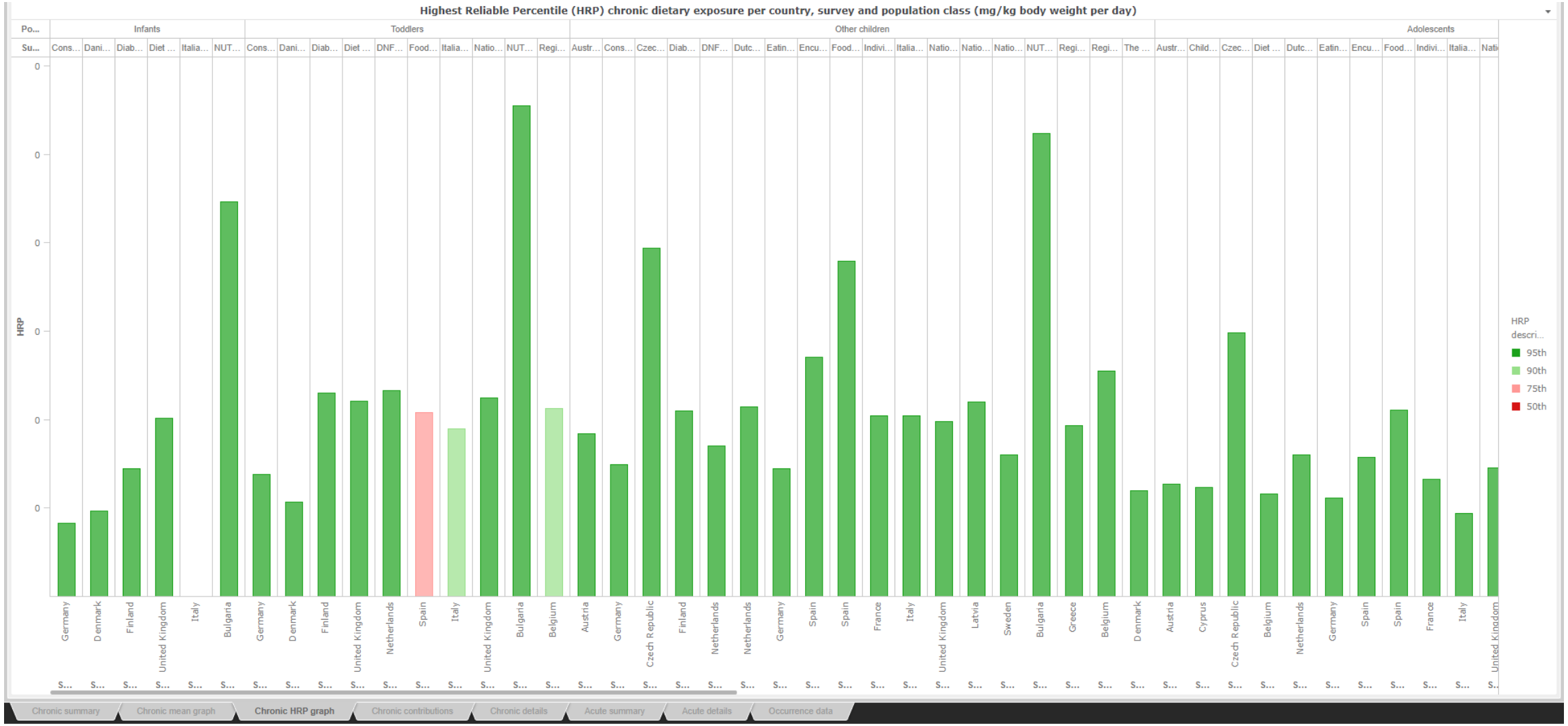
CHRONIC assessment

- Only surveys of more than one day are considered
- For each individual, the total relevant residues will be combined with the average daily consumptions of the corresponding food commodities, and the resulting exposures per food will be summed to obtain the total individual chronic exposure
- The mean and the higher percentile (usually the 95th percentile) of the individual exposures is calculated for each dietary survey and each age class separately

FACE – **Example 1**

European Food Safety Authority

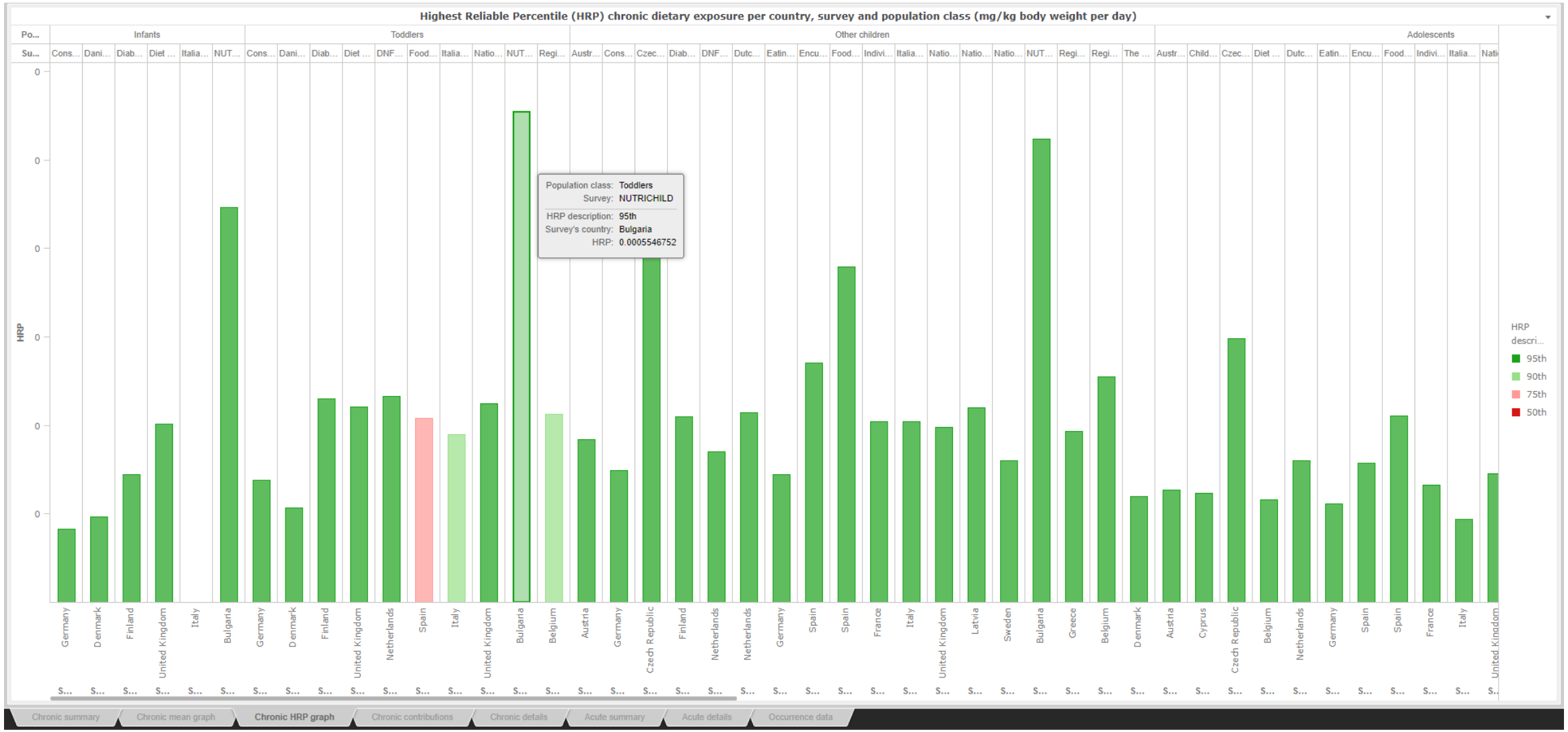
CHRONIC assessment – DETAILS PER SURVEY



FACE – **Example 1**

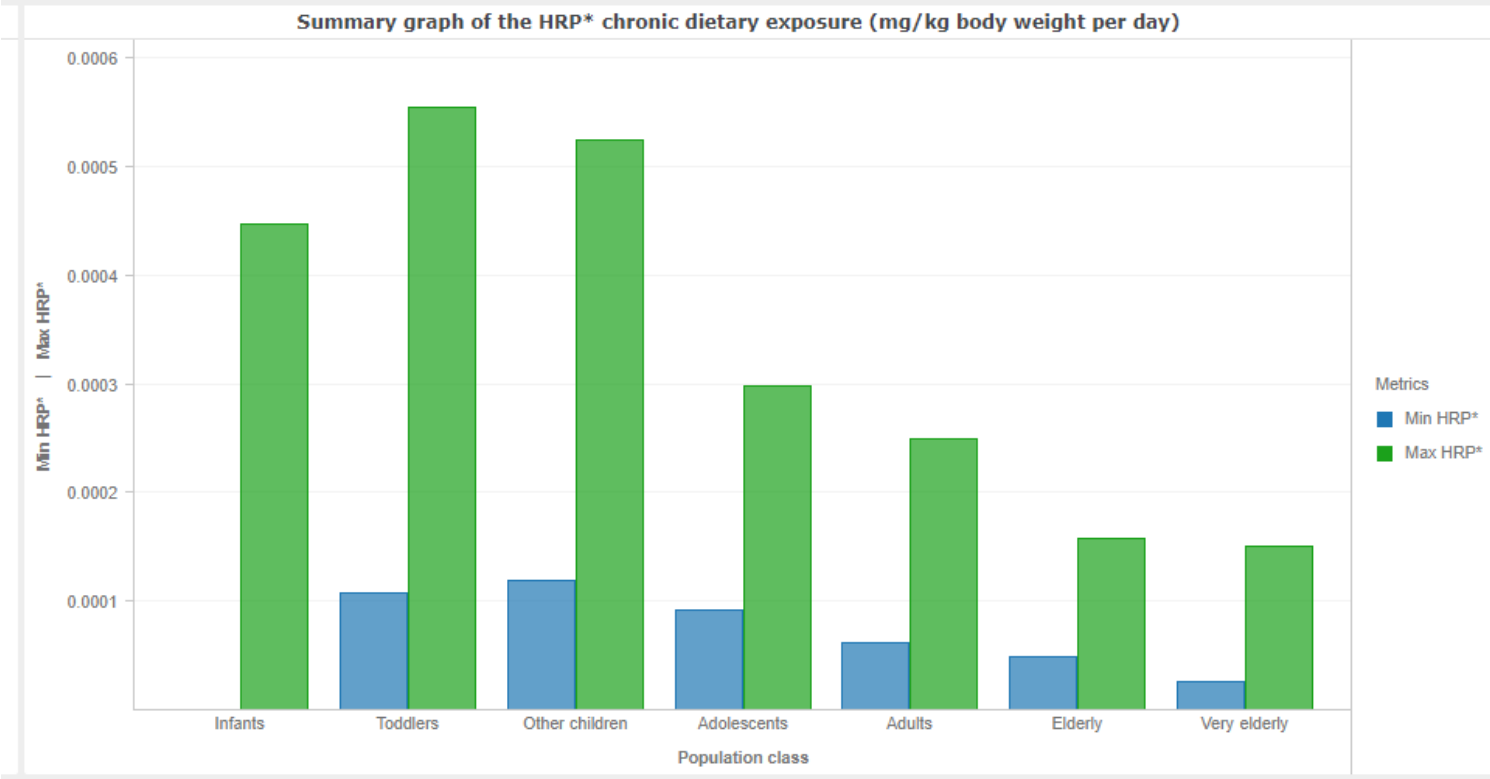
European Food Safety Authority

CHRONIC assessment – DETAILS PER SURVEY



CHRONIC assessment – SUMMARY

- The minimum and the maximum values of the highest reliable percentile per age class is reported in the summary graph.



CHRONIC assessment – Comparison with ADI

Table 2. Chronic dietary exposure of consumers - Summary statistics across European dietary surveys

Population class	Number of surveys	Highest exposure estimate (mg/kg bw per day)	% ADI
Infants	6	0.0004	7%
Toddlers	10	0.0006	10%
Other children	18	0.0005	8%
Adolescents	17	0.0003	5%
Adults	17	0.0002	3%
Elderly	14	0.0002	3%
Very elderly	12	0.0002	3%

Acceptable Daily Intake: 0.006 mg/kg bw

FACE – **Example 1**

CHRONIC assessment

Food basket of Reg. (EC) No 429/2008 VS FACE

Table 3. Chronic exposure of consumers based on residue data in tissues of chickens for fattening **calculated following the food basket of Regulation (EC) No 429/2008** (**only adult**)

	Liver	Kidney	Muscle	Skin/fat	Sum
TRC + 2SD (mg/kg)	0.618	0.190	0.033	0.301	
Consumption (g/day)	100	10	300	90	
DITR (mg/day)	0.0618	0.0019	0.0099	0.0271	
% ADI	**17**	**1**	**3**	**8**	**29**

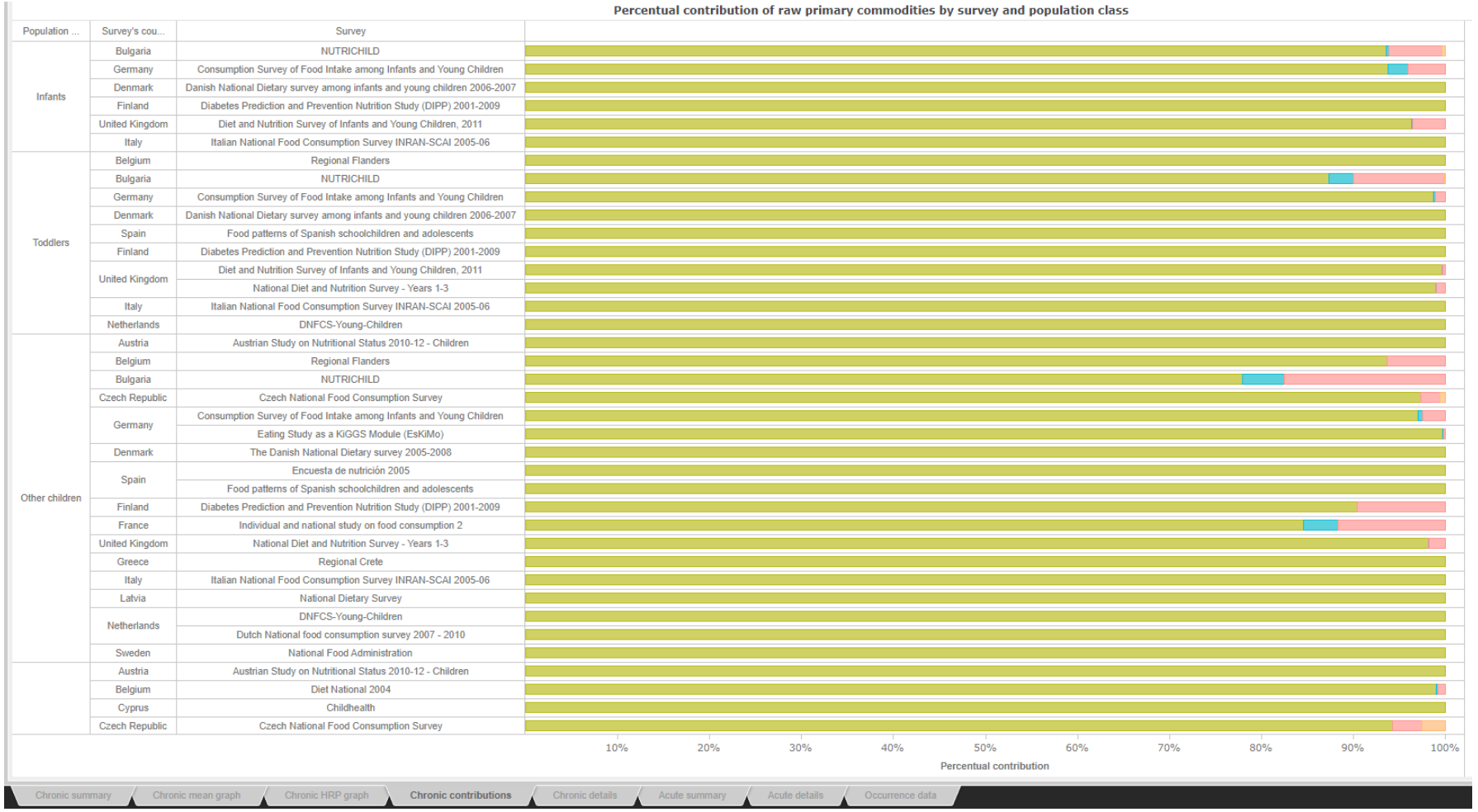
TRC: total residue concentration; SD: standard deviation; DITR: Dietary intake calculated from total residues

29% Reg. 429/2008 (JECFA) VS 3% FACE

efsa
European Food Safety Authority

CHRONIC assessment

Contribution of tissues/products to expsoure



FACE – **Example 2**

CHRONIC assessment

Another example

FACE – **Example 2**

CHRONIC assessment

Table 4. Total residues in tissues/products of chickens for fattening and laying hens administered xx mg additive/kg feed

	Liver	Kidney	Muscle	Skin/fat	Whole egg
TRC + 2SD (mg/kg)	7.87	2.14	0.40	2.49	8.95

The residue concentration in muscle and skin/fat will be applied to the intake of meat at the following proportions: 90% muscle and 10% skin/fat. This corresponds to 0.609 mg/kg.

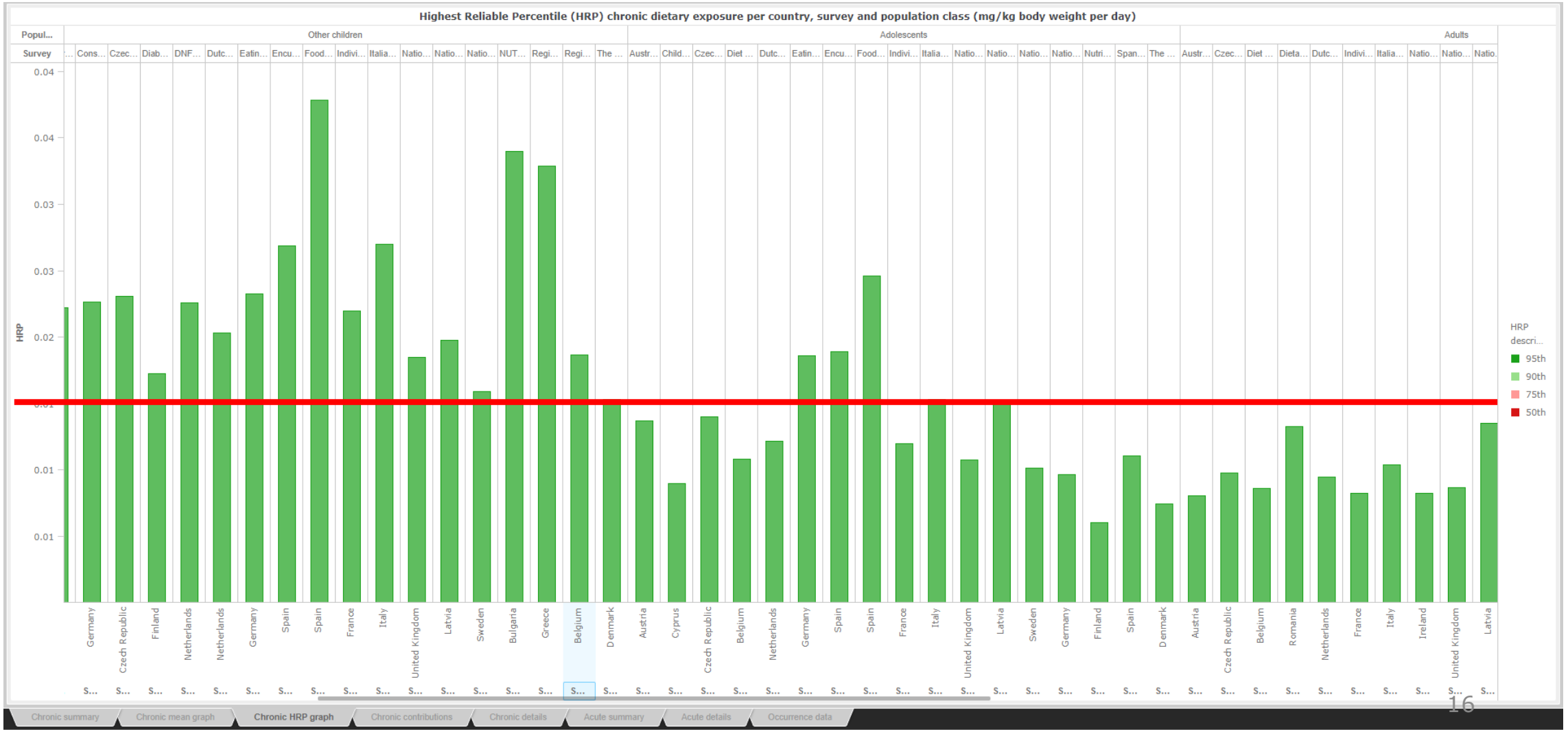
Raw Primary Commodity	Metrics	Occurrence level (mg/kg)
Birds fat tissue	A0F1E	2.49
Birds liver	A16YS	7.87
Birds meat	A0EYG	0.609
Birds offals and slaughtering products (other than liver)	A16YV	2.14
Fish (meat)	A026V	0.000000
Honey	A033J	0.000000
Mammals fat tissue	A0F3G	0.000000
Mammals liver	A0F3J	0.000000
Mammals meat	A0EYF	0.000000
Mammals offals and slaughtering products (other than liver)	A16YT	0.000000
Milk	A02LT	0.000000
Seafood	A16YX	0.000000
Whole eggs	A031F	8.95

Submit

FACE – **Example 2**

CHRONIC assessment – Detailed results

ADI



CHRONIC assessment – Summary

Table 5. Chronic dietary exposure of consumers - Summary statistics across European dietary surveys

Population class	Number of surveys	Highest exposure estimate (mg/kg bw per day)	% ADI
Infants	6	0.0318	212
Toddlers	10	0.0356	237
Other children	18	0.0379	253
Adolescents	17	0.0246	164
Adults	17	0.0135	90
Elderly	14	0.0118	79
Very elderly	12	0.0147	98

efsa
European Food Safety Authority

CHRONIC assessment

Food basket of Reg. (EC) No 429/2008 vs FACE

Table 6. Chronic exposure of consumers based on residue data in tissues and products of chickens for fattening/laying hens **calculated following the food basket of Regulation (EC) No 429/2008 (only adult)**

	Liver	Kidney	Muscle	Skin/fat	Whole egg	Sum
TRC + 2SD (mg/kg)	7.87	2.14	0.40	2.49	8.95	
Consumption (g/day)	100	10	300	90	100	
DITR (mg/day)	0.79	0.02	0.12	0.22	0.89	
% ADI	**88**	**2**	**13**	**24**	**99**	**226**

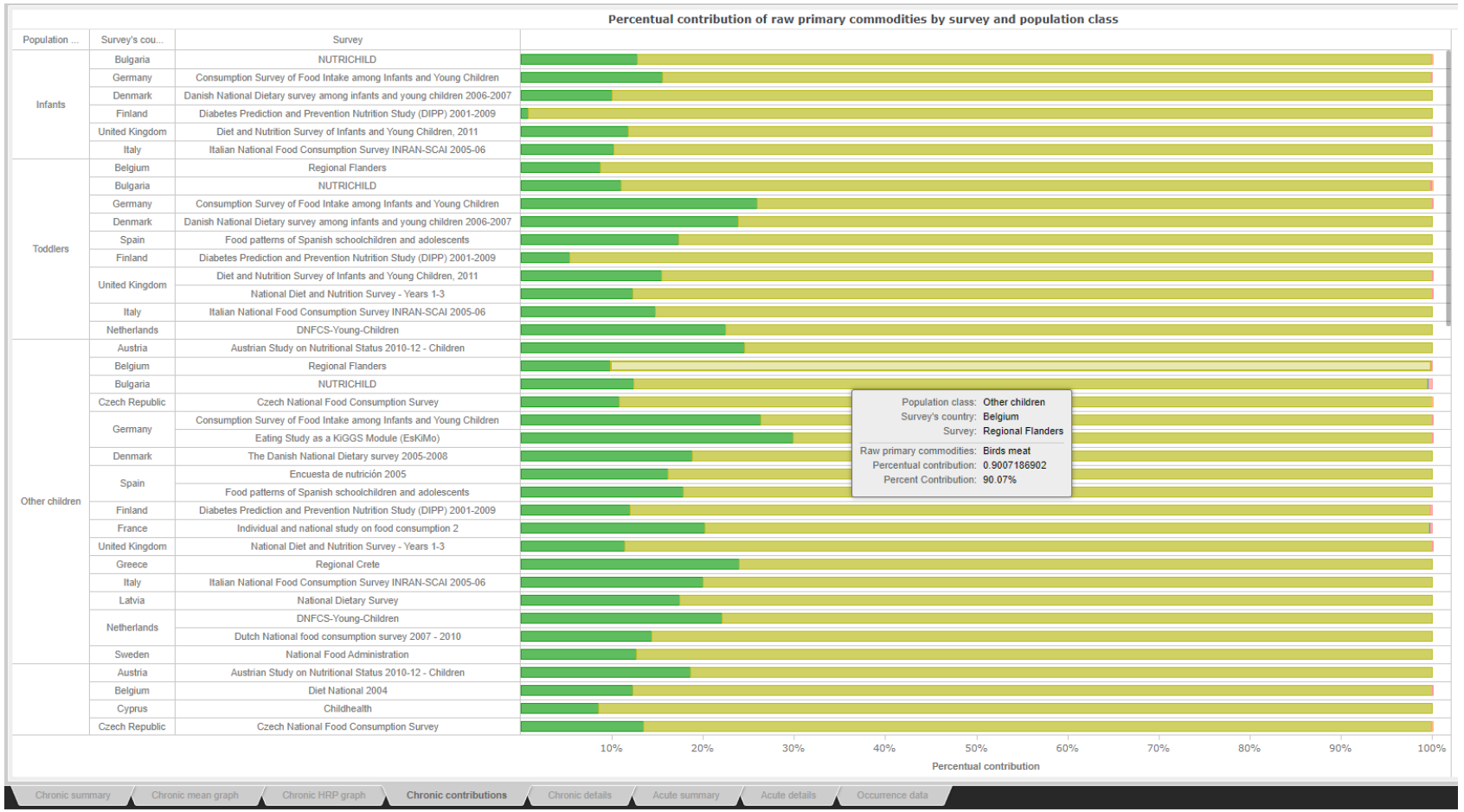
TRC: total residue concentration; SD: standard deviation

226% Reg. 429/2008 (JECFA) VS 90% FACE

European Food Safety Authority

CHRONIC assessment

Contribution of tissues/products to exposure



FACE – How to interpret the results: ACUTE

ACUTE assessment

- the total relevant residue for each food commodity will be combined with the total corresponding consumption within each single day to obtain the acute exposure
- The higher percentile (usually the 95th percentile) exposures based on the consuming days only will be calculated for each food commodity, dietary survey and age class separately.

Raw primary commodity	Population class	Number of surveys	Highest exposure estimate (mg/kg bw per day)	% ADI
Birds fat tissue	Toddlers	1	0.00022	4
Birds fat tissue	Other children	4	0.00027	4
Birds fat tissue	Adolescents	2	0.00027	5
Birds fat tissue	Adults	8	0.00020	3
Birds fat tissue	Elderly	4	0.00008	1
Birds fat tissue	Very elderly	3	0.00010	2
Birds liver	Infants	2	0.00093	15
Birds liver	Toddlers	1	0.00046	8
Birds liver	Other children	7	0.00340	57
Birds liver	Adolescents	4	0.00169	28
Birds liver	Adults	12	0.00300	50
Birds liver	Elderly	6	0.00074	12
Birds liver	Very elderly	4	0.00030	5
Birds meat	Infants	5	0.00078	13
Birds meat	Toddlers	11	0.00073	12
Birds meat	Other children	20	0.00093	15
Birds meat	Adolescents	20	0.00057	10
Birds meat	Adults	23	0.00042	7
Birds meat	Elderly	16	0.00035	6
Birds meat	Very elderly	14	0.00034	6
Birds offals and slaughtering products (other than liver)	Adults	3	0.00045	7

Concluding remarks

- Data requirements are the same (residue studies, full toxicological dataset)
- Applicants are invited to follow Reg. (EC) No 429/2008 and the updated Guidance on consumer safety (2017)
- Chronic vs Acute assessment is based on the toxicological effects of the additive
- FACE relies on a more realistic consumption data and covers all age classes and different European countries
- High consumers are protected
- The detailed results (per country per survey) allows to have a full picture on the exposure of consumers in Europe

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
@plants_efsa
@methods_efsa