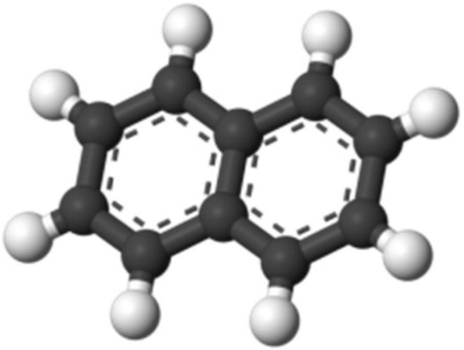
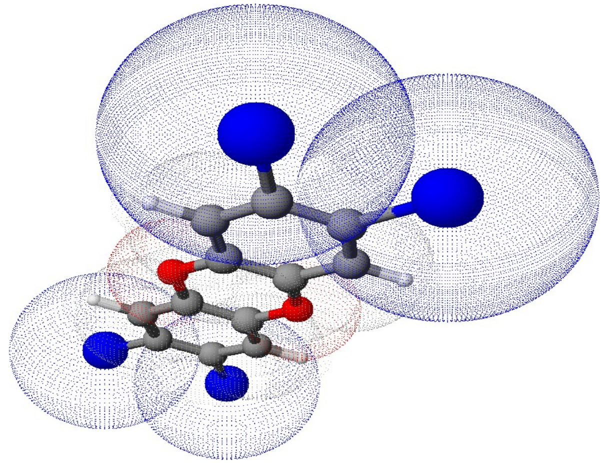


ESTIMATION OF MEASUREMENT UNCERTAINTY FOR ORGANIC ENVIRONMENTAL CONTAMINANTS

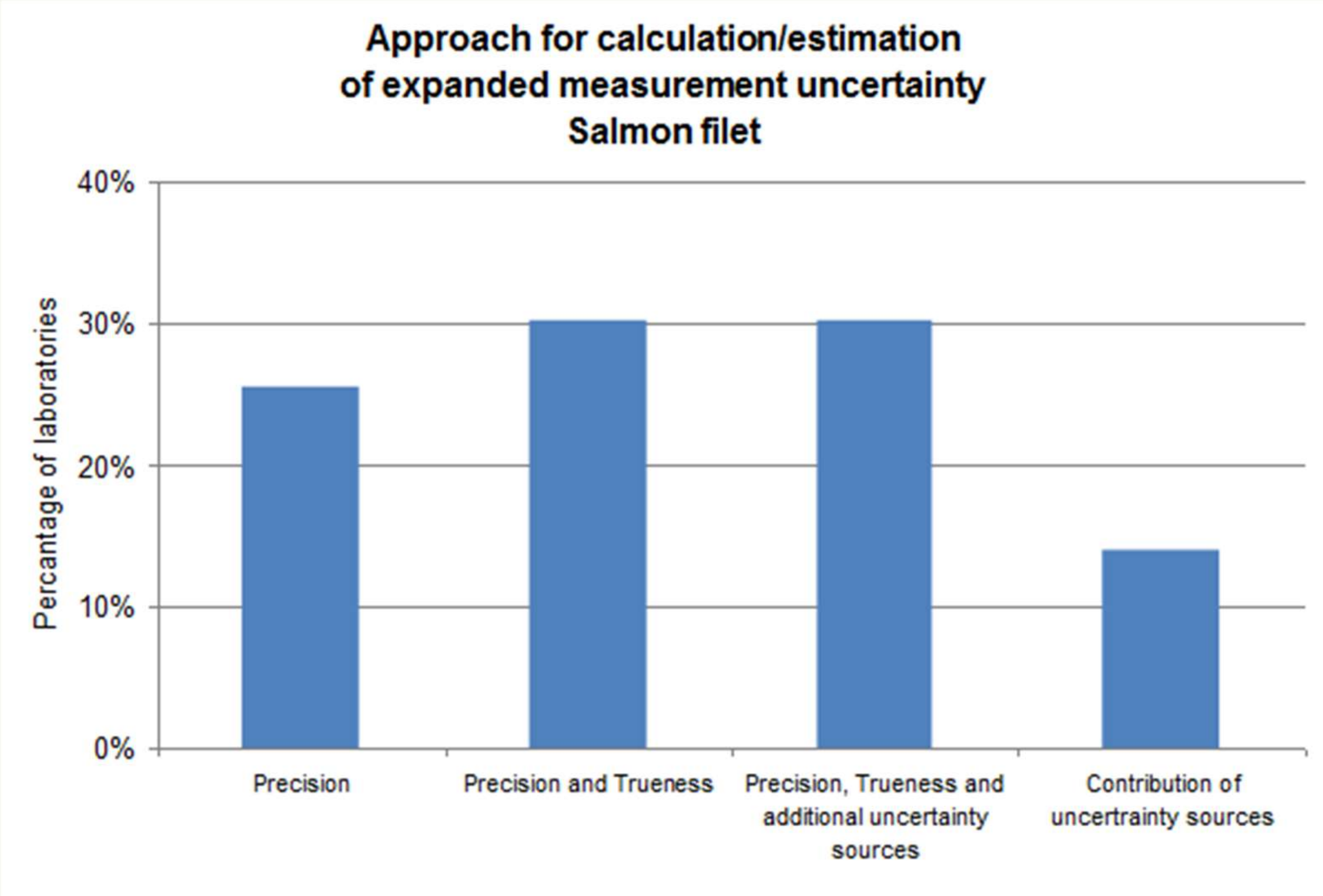
(MU GUIDANCE FOR DIOXINs & PCBs)



Background

- Quality Control assessment of PT scheme data
- Possible misinterpretation of the Regulation MU requirement by some labs
- General desire to harmonise (with better control) methodologies
- Complexity of Dioxin methodology & MU estimation

NRL network survey



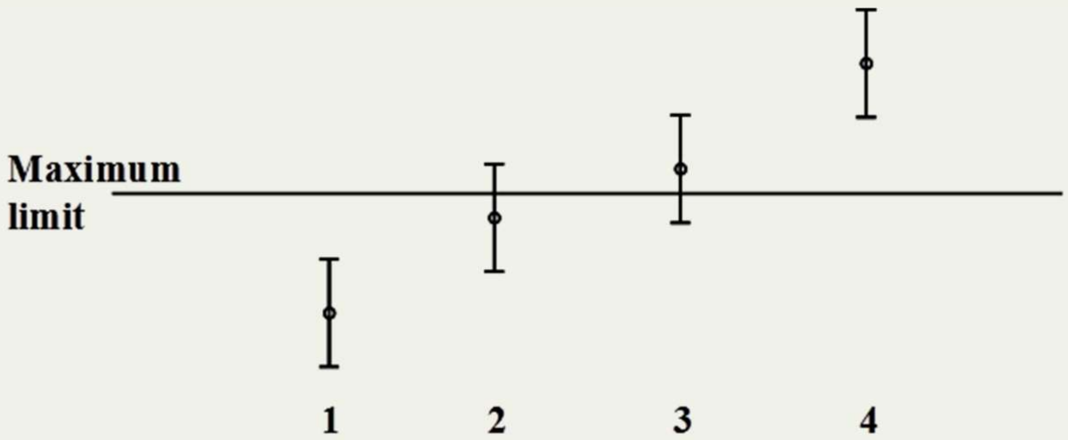
Source: EURL-NRL workshop report

CWG on Measurement Uncertainty (MU)

- Created to address the issues seen in reporting MU
- Assess the different approaches used in the network and identify suitable approach(es)
- Produce a guidance document (Santé) for the estimation of MU within the network
- Criteria based

Some basics for OC

- *Reported analytical results will take the form 'x ± U', where x = best estimate of the true value and U the expanded measurement uncertainty.
- Regulatory context



* ISO/IEC 17025:2005 [ISO/IEC 17025:2005-08, /14/] & Regulation(EU) No 589/2014 (food), (EC) No 152/2009 (feed)

Approaches Considered for Dioxins & PCBs

- Empirical or top-down approach based on performance data of the whole method taking into account trueness and precision contributions
- Theoretical or bottom-up approach based on a mathematical model of the measurement process, estimating individual contributions of the relevant sources of uncertainty
- Semi-empirical approach based on a combination of the theoretical and empirical approach

Contributions from Current Performance

- Historical (e.g. during validation) precision and bias studies provide a valid “snapshot” of laboratory & method performance and their contributions to MU
- However in routine analysis, anomalies such as: extraction issues, low recoveries, insufficient purification, injections of “dirty” sample extracts, poor resolution during chromatographic separation and GC-MS sensitivity problems, do occur
- Thus, incorporation of current performance would provide a more realistic MU estimate

Empirical Approach Requirements

- Intermediate precision data
- Trueness (or bias) data (e.g. from CRMs, PTs etc.)
- Daily performance element (LOQ and daily QC)
- Analytical result

Semi-empirical Approach Requirements

only recommended for laboratories new to the field

- Intermediate precision data
- Bias data from fortification experiments
- Calibration Curve Uncertainty
  - Additional Contributions
    - Volume uncertainty
    - Standard solution concentration uncertainty
    - Sample aliquot weighing uncertainty
    - Others

Empirical approach procedure

Two-stage process

1. Calculation of combined standard uncertainty factor from precision, bias (from PTs) and other relevant data (e.g. large concentration range data, standards, etc.)

Empirical approach procedure-2

- Stage 2- Application of uncertainty factors to real sample measurements, incorporating current LOQ (and QC data)
- Dynamic LOQ (calculated in each set/batch from Blank) – incorporates recovery

Formulas

$$\text{Combined U factor - } u = \sqrt{(U_{Rw})^2 + (U_{Bias})^2 + (U_{\text{linearity response}})^2 + (U_{\text{stds.}})^2}$$

$$MU\ (\%) = k * \frac{\left(\sqrt{(LOQ)^2 + conc.^2 * u_{factor}^2}\right)}{conc.} * 100$$

MU for the sum TEQ is propagated from the individual congener MU data using the RSS (Square root of the TEF weighted sum of squares) approach.

$$u_c(TEQ = TEF_1 \cdot u_{c1} + \cdots + TEF_{29} \cdot u_{c29}) = \sqrt{\sum_{i=1}^{29} (TEF_i \cdot u_{ci})^2}$$

Example (dioxin data)

A: Calculation of combined std. uncertainty factor-1

Uncertainty component – intermediate precision (20 data sets required)

IHRM															
		1691	1692	1696	1703	1704	1707	1708	1724	1728	1732	1733	Current	**Mean**	**Uncert.**
															uRw
	2378-TCDD	0.44	0.44	0.49	0.48	0.42	0.42	0.49	0.51	0.47	0.43	0.49	0.43	0.46	**0.073**
	12378-PCDD	0.27	0.28	0.30	0.27	0.24	0.24	0.29	0.24	0.28	0.25	0.28	0.28	0.27	**0.068**
	123478-HCDD	0.02	0.01	0.01		0.01	0.01	0.01	0.02	0.02	0.01	0.01	0.01	0.01	**0.420**
	123678-HCDD	0.92	0.89	0.94	0.86	0.80	0.83	0.87	0.89	0.90	0.81	0.89	0.91	0.86	**0.056**
	123789-HCDD	0.21	0.19	0.20	0.20	0.16	0.17	0.20	0.20	0.19	0.18	0.19	0.18	0.19	**0.080**

e.g. uRw = std dev of difference ratios/ √ no. of measurements

Remove any seriously outlying data

A: Calculation of combined std. uncertainty factor-2A

(Example) Uncertainty component - Bias using CRM

	1292	1293	1298	1299	1300	1301	1302	1304	1305	1306	**CRM value**	Uncert. from CRM
ng/kg												u_{bias}
2,3,7,8-TCDD	0.53	0.55	0.48	0.51	0.51	0.54	0.61	0.57	0.52	0.52	**0.53**	0.0684
1,2,3,7,8-PeCDD	0.26	0.24	0.24	0.26	0.27	0.27	0.29	0.24	0.26	0.27	**0.24**	0.0685
1,2,3,4,7,8-HxCDD	0.01	0.03	0.01	0.02	0.01	0.02	0.04	0.01	0.02	0.01	**0.02**	0.5738
1,2,3,6,7,8-HxCDD	0.56	0.72	0.62	0.80	0.77	0.71	0.71	0.71	0.73	0.68	**0.70**	0.0984
1,2,3,7,8,9-HxCDD	0.08	0.10	0.08	0.13	0.14	0.08	0.15	0.09	0.11	0.11	**0.11**	0.2415

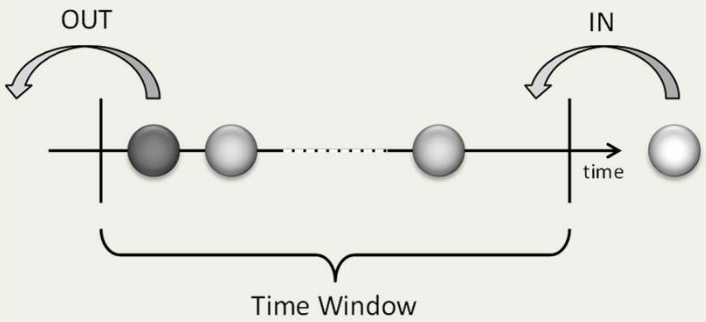
A: Calculation of combined std. uncertainty factor- 2B - Example

Uncertainty component - Bias using PT data

Min 6 participations required

		Assigned value ng/kg			Reported Value ng/kg			Uncertainty of assigned value uCref,1			Factor u_{bias}
	TEF	PT1	PT2	PT3	PT1	PT2	PT3	uCref,1	uCref,2	uCref,3	
Congeners		Halibut	Fish oil	Palm oil	Halibut	Fish oil	Palm oil	Halibut	Fish oil	Palm oil	
2,3,7,8-TCDD	1	0.957	0.385	0.074	0.9	0.38	0.08	0.024	0.012	0.003	0.030
1,2,3,7,8-PeCDD	1	0.656	0.195	0.163	0.64	0.2	0.16	0.017	0.008	0.007	0.030
1,2,3,6,7,8-HxCDD	0.1	1.05	0.56	0.335	1.04	0.54	0.34	0.018	0.015	0.008	0.020

Rolling Time window scheme



A: Example Calculation of std. combined uncertainty factor-3

Uncertainty component – at different concentrations (for RA or research studies)

Fortified matrix data

Concentration - ng/kg	milk	milk + 0.2	milk + 0.8	milk + 4.0	milk + 50	fish	fish +1.5	fish +8.0	fish + 50	fish + 125
2378-TCDD		0.19	0.79	3.93	41.03	0.15	1.28	6.21	38.75	94.68
12378-PCDD		0.19	0.92	4.50	53.14	0.06	1.52	7.63	45.21	121.48
123478-HCDD		0.20	0.92	4.50	52.91	0.07	1.37	7.40	44.34	118.43
123678-HCDD		0.21	0.93	4.84	55.94	0.06	1.49	7.79	46.97	123.44
123789-HCDD		0.20	0.95	5.06	56.27	0.02	1.33	8.11	44.68	109.75
Exp'td Level	nil	0.20	0.80	4.00	50.00		1.50	8.00	50.00	125.00

Difference ratios

	milk	milk + 0.2	milk + 0.8	milk + 4.0	milk + 50	fish	fish +1.5	fish +8.0	fish + 50	fish + 125	**Uncert.** u_{bias}
2378-TCDD		4.04	1.48	1.72	17.93		14.74	22.33	22.50	24.26	**0.033**
12378-PCDD		6.11	15.46	12.53	6.29		1.16	4.61	9.58	2.82	**0.016**
123478-HCDD		0.56	14.50	12.57	5.83		8.77	7.44	11.31	5.26	**0.015**
123678-HCDD		4.92	16.70	21.08	11.88		0.91	2.61	6.05	1.25	**0.025**
123789-HCDD		0.79	18.82	26.38	12.54		11.51	1.32	10.63	12.20	**0.028**

A: Calculation of combined std. uncertainty factor

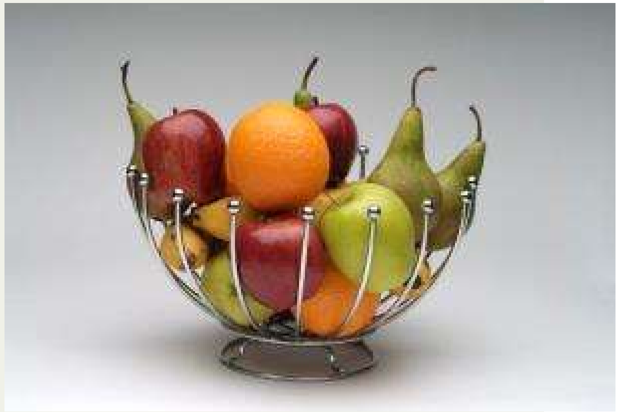
	U precision	U bias	U lin. resp	U stds	Combined Standard U factor
2378-TCDD	0.073	0.030	0.018	0.025	**0.085**
12378-PCDD	0.068	0.030	0.020	0.025	**0.081**
123478-HCDD	0.420	0.013	0.021	0.025	**0.422**
123678-HCDD	0.056	0.020	0.017	0.025	**0.067**
123789-HCDD	0.080	0.033	0.011	0.025	**0.091**

Combined U factor - $u = \sqrt{(U_{Rw})^2 + (U_{Bias})^2 + (U_{linearity\ response})^2 + (U_{stds.})^2}$

B: Calculation of expanded measurement uncertainty (including current performance)

$$MU\ (\%) = k * \frac{\left(\sqrt{(LOQ)^2 + conc.^2 * u_{factor}^2}\right)}{conc.} * 100$$

	LOQ ng/kg	Measured Concentration ng/kg	U factor	Measurement Uncertainty %
2378-TCDD	0.04	<0.06	0.085	**138**
12378-PCDD	0.07	0.57	0.081	**29**
123478-HCDD	0.05	0.45	0.422	**88**
123678-HCDD	0.21	1.08	0.067	**43**
123789-HCDD	0.08	0.45	0.091	**39**



Application to TEQ

	LOD/sample weight ng/kg	Measured Concentration ng/kg	Std. U factor	Measurement Uncertainty %	TEQ ng/kg
2378-TCDD	0.04	<0.06	0.085	**138**	0.06
12378-PCDD	0.07	0.57	0.081	**29**	0.57
123478-HCDD	0.05	0.45	0.422	**88**	0.05
123678-HCDD	0.21	1.08	0.067	**43**	0.11
123789-HCDD	0.08	0.45	0.091	**39**	0.05

		Lower range	1.32
For Sum TEQ	**14.9**		**1.45**
		Upper range	1.78

$$u_c(TEQ = TEF_1 \cdot u_{c1} + \cdots + TEF_{29} \cdot u_{c29}) = \sqrt{\sum_{i=1}^{29} (TEF_i \cdot u_{ci})^2}$$

Conclusions

- The CWG recommends the use of the empirical (top-down)approach incorporating intermediate precision and bias components
- The introduction of the daily or current contribution to MU provides a more realistic estimate
- The guidance document is criteria based and allows labs to tailor their approaches to estimating MU

Thank You