The K.M-method, (also compared to a worst and best-case scenario)

The KM-method is non-parametric, which means that it does not assume an underlying distribution in the data. The KM method estimates the contribution of the non-detects based on a ranked order of the risk of both detected and non-detected compounds in an individual sample (Bolks et al., 2014; Helsel, 2012, 2010). Using the KM method the average risk-contribution of all compounds is calculated and is then multiplied with the number of mixture components to estimate the total risk from the mixture.

Table 1 outlines a five component mixture where the respective TU (MEC/WQO) contribution is based either on a measured concentration (compounds A, C and E), or based on worst case estimates (i.e. non-detects are present at their individual LOD) (compounds B and D). The percentiles needed to estimtae the average risk is determine for the three different scenarios used in the article. In scenario one all non-detects are assumed to be present at their corresponding LOD (a worst case scenario). In the second scenario non-detects are assumed to have a concentration of zero (a best case scenario). In scenario three the KM method is used to include non-detects in the risk estimate.

The percentiles are in turn calculated; for the 'non-detect = LOD' by dividing 1 with the number of analyzed components in the mixture (5). For the 'non-detect = 0' by dividing 1 with the number of detected compounds (3). For the KM method the percentile for each detected compound is determined by; the number of observations which are below the specific TU-value, divided with the number of values below or at that specific value, multiplied with the previous percentile.

For the first detect this equates to; the number of observations which are below the specific TU-value (4), divided with the number of values below or at that specific value (5), multiplied with the previous percentile (1), (4/5*1=0.8).

Within the NADA package used to determine the KM-average, and subsequent total risk the compound that has the lowest potential TU-contribution (compound E in the example) will by default be assumed to be a detect.

For the second detect there are three observations which are known to be at, or below, that specific TU-value. Therefore the percentile value is determined as the number of values below the specific value (2) divided with the number of values below or at that specific value (3) multiplied with the previous percentile (0.8), (2/3*0.8≈ 0.53). From the percentiles the average risk contribution is then calculated.

In order to visualize the process figures 1a-c shows the distribution as determined in Table 1 for the three different scenarios, and the average contribution is reported as the area under the curve (AUC) in Table 2.

Table 1. A hypothetical five compound mixture where compound B and D are non-detects. The percentiles used to determine the average risk contribution under a worst-case, KM, or best case scenario are also given.

Compound	Sign	TU	Percentile nondetect = LOD	Percentile nondetect = 0	Percentile KM
A	=	0.50	0.80	0.67	0.80
B	<	0.25	0.60	-	-
C	=	0.15	0.40	0.33	0.53
D	<	0.10	0.20	-	-
E	=	0.05	0.00	0.00	0.00

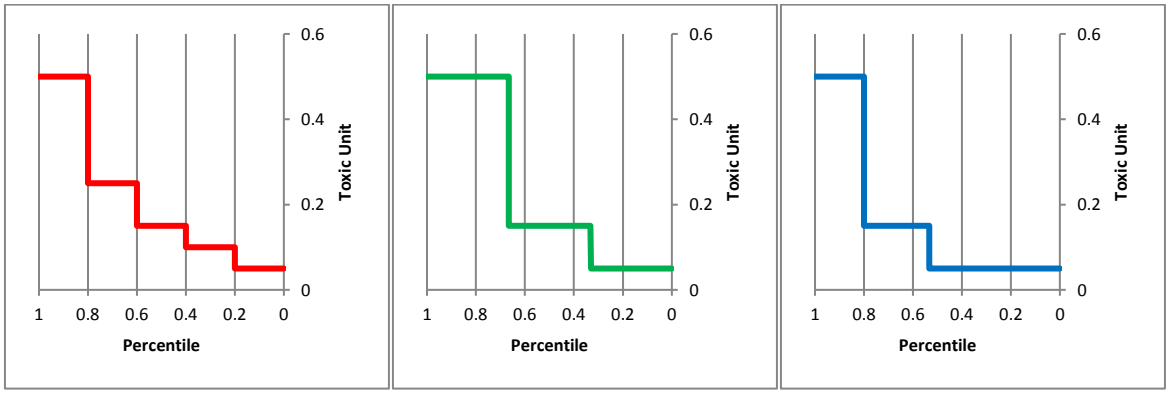

Figure 1a-c: A graphical display of the risk distributions from the hypothetical mixture in table 4 under a) worst-case b**)** best case and c) KM-adjusted scenario.

It should be noted that the KM method excludes all non-detects which (if present at their individual LOD) would have contributed more to the total risk than the largest risk contribution from a detected compound. For example, a non-detect Â which at its LOD would contribute 0.6 TU would be excluded from the KM-method and from the best-case scenario, but included in the worst-case scenario.

Table 2: The average risk contribution per compound, number of compounds and total estimated risk for the hypothetical mixture defined in table 4 for a worst-case, KM and best case scenario.

	Area Under Curve (Average risk contribution)	n	Sum of TU
Non-Detect Present at LOD	0.21	5	1.05
Non-Detect KM Adjusted	0.17	5	0.83
Non-Detect Not Present	0.23	3	0.70