What's new in MCRA 7.1?

This note describes MCRA 7.1 (release date 19 December 2011).
The point of comparison is MCRA 7.0 as described in the Reference Manual 2010-08-25.

Summary of changes:

1. Method LNN for estimating usual intake (chronic risk assessment) has been upgraded to include the estimation of a correlation between intake frequency and intake amount. This is similar to the NCI model described in Tooze et al. (2006).
2. The original LNN method in MCRA 7.0 has now been renamed LNN0, where the '0' indicates the absence of correlation.
3. The LNN0 model is now fitted by maximum likelihood, employing Gauss-Hermite integration, instead of by the approximate maximum likelihood routine GLMER in the R package.
4. For chronic models amount are usually transformed before the statistical model is fit. The power transformation, given by y^p, has been replaced by the equivalent Box-Cox transformation. The Box-Cox transformation is a linear function of the power transformation, given by $(y^p-1)/p$, and has a better numerical stability.
5. A more accurate way of back-transforming intake amounts has been implemented for the LNN, LNN0 and BBN models with a Box-Cox transformation (Gauss-Hermite integration instead of a Taylors series expansion). This is in agreement with Dekkers et al. (in prep.).
6. A new method to estimate individual usual intakes has been added to BBN and LNN0. The method builds on the proposal of Kipnis et al. (2009), but is modified to ensure that the population mean and variance are better represented. The method is based on shrinkage of the observed individual means (modified BLUP estimates) and shrinkage of the observed intake frequencies. Individual intakes are not yet available for LNN, and when a covariable is modelled by a spline function of degree higher than 1. The individual usual intake distribution applies to the population for which the consumption data are representative, and automatically integrates over any covariates present in the model.
7. In case of a model with covariates the usual intake was presented in graphs and tables as a function of the covariates (conditional usual intake distributions). In addition, there is now also a marginal usual intake distribution which applies to the population for which the consumption data are representative.

8. When a chronic model is applied to consumption data with just one day per person, MCRA will ask for the input of a variance ratio for the amount model and a dispersion factor for the frequency model. These values can for example be taken from the output of similar exposure assessments of datasets with multiple days per person.
9. An option has been added to correct for measurement uncertainty. Concentration data are variable because of sampling error, but also because of analytical error. The amount of analytical error is commonly quantified as measurement uncertainty. If the measurement uncertainty of the concentration data is known it can be subtracted from the total variance in the data (to a minimum of 0). For measurement uncertainty MCRA will suggest a coefficient of variation (CV) based on the Horwitz equation and the mean level of the compound over all available concentration data. When analytical error is reported by the analytical laboratory, then this information should be used (CV, as %).
10. An option has been added to enter a limit value for exposure (e.g. a value from the PRIMO software). This is shown for comparison purposes in the output together with the results of probabilistic modelling (table with percentiles, cumulative and exceedance distribution graphs)
11. A pie chart with contributions to the tail has now been added for BBN and LNN0 based on the individual intakes.
12. Detailed information on frequencies and amounts when cofactors are specified (before only output for the total population was available).
13. In the conversion algorithm a check is now made on the simultaneous use of Food conversion factors for weight changes between food and eRAC (step 3 of the conversion algorithm) and processing factors for concentration changes between RAC and eRAC (step 2 of the conversion algorithm). If the same code pair is found in both tables, the processing factor is modified to indicate the change in amount (rather than concentration) of the compound.
14. For an acute risk assessment, the drill-down output has been improved. Detailed information about variability factors and stochastic variability factors has been added to the information about the mixture sample and subportion concentration.
15. For a chronic risk assessment a drilldown has been added showing the consumed amount per commodity for day 1, 2, ... in the survey, the mean concentration per commodity, the mean and individual usual intake of nine consumers.
16. All exposure output in tables and graphs is now also specified in % of limit value (ARfD or ADI) and on a Margin of Exposure Scale (when the limit value is available).

17. Exposure levels are determined automatically or specified manually. When manually is chosen, levels are specified as absolute values or as percentages.
18. It is now possible to account for different processing types in the unit variability models (related to bulking/blending) even if the model is run without processing factors.
19. For unit variability models based on the lognormal distribution, the drawn residue for a unit may be based on a mean value that is a) unbiased or b) biased at the log-scale. The last option is added to the interface. For the Bernoulli distribution an option 'realistic' is added meaning that drawn residues will become zero in the majority of units (censoring or not).
20. Several bugs were corrected.

Note: In a future version MCRA will also include the functionality of the IPRA (Integrated Probability Risk Assessment) program. As a preparation to this development IPRA is already made available in a web-based environment, for the moment separated from the MCRA website (using a diffent url), although both programs share the same underlying code. Data for IPRA are uploaded as Excel-files.

LNN model with correlation for Chronic Risk Assessment

The LogisticNormal-Normal (LNN) model can now allow for a correlation between frequency and amount at the individual level. This model is also known as the NCI model. The model is appropriate in situations where individuals with frequent intakes have a higher intake than individuals with less frequent intakes. The MCRA plot "FREQ vs AMOUNT" might indicate that this is the case as this plot depicts the distribution of the mean intake for individuals with an intake on one day (out of two days), and the distribution for individuals with an intake on two days. The LNN model without correlation is now termed LNN0.

The model can be fitted by choosing "logistic/normal with correlation (LNN)" in the second step (i.e. Specify Model) of an MCRA analysis. The output is almost identical to the output of the LNN0 model. An estimate of the correlation is given in the "Additional output", along with an approximate (see technical note) likelihood ratio test for the null hypothesis that the correlation equals zero. One can switch between the output of the LNN model with and without correlation by using the link in the lower left part of the output screen.

The LNN0 model can be set up to automatically select an appropriate polynomial (e.g. linear or quadratic) for a covariate such as age. The LNN model only fits the polynomial which is chosen by LNN0. The transformation of the positive amounts (logarithmic or Box-Cox) is the same in both models.

Technical notes for LNN model with correlation:

1. The LNN model with correlation is fitted by means of maximum likelihood. This requires integration over the bivariate individual random effects which is accomplished with bivariate Gauss-Hermite numerical integration. Gauss-Hermite integration approximates the integral by a weighted sum of carefully chosen function evaluations at so-called integration points. The number of integration points determines the level approximation, currently 10 integration points are used in each dimension, giving 100 integration points in total. It is not yet clear whether 10 integration points suffices in most cases.
2. The likelihood is optimized by means of the Simplex routine which stops when the smallest and largest likelihood values at the simplex have a relative difference less than 1.0e-6. The maximum number of function evaluations in the Simplex algorithm is set to 1500. The Simplex algorithm starts at the parameter estimates of the LNN0 model with the correlation parameter set to zero.
3. The "Additional output" gives the value of the log-likelihood for the LNN0 estimates and for the LNN estimates. The difference between the two likelihoods is shown, which can be used for a likelihood ratio test to test the statistical significance of the correlation between frequencies and amounts. Note that the issue is not significance of the correlation but relevance.
4. The back transformation to usual intake employs Gauss-Hermite numerical integration with 30 integration points. Note that this is only relevant for the Box-Cox transformation since for the log transformation an exact back transformation is used.
5. The individual usual intake is not yet calculated in the LNN model (where correlation between frequencies and amounts is modelled).

Back transformation to usual intake

In case a power or Box-Cox transformation is used in LNN or BBN the usual intake of an individual has to be back transformed to the original scale. This involves integration over the within individual random effect. In version 7.1 the integration is carried out by means of Gauss-Hermite numeric integration with 30 integration points, instead of a two-term Taylor approximation. Numeric integration is much more accurate especially when the power is small. Note that for the logarithmic transformation an exact back transformation was already employed.

References

Dekkers ALM, Ocké MC, Slob W (in preparation) An efficient method for backtransformation of usual intakes in dietary exposure assessment.

Kipnis V, Midthune D, Buckman DW, Dodd KW, Guenther PM, Krebs-Smith SM, Subar AF, Tooze JA, Carroll RJ, Freedman LS (2009). Modeling data with excess zeros and measurement error: Application to evaluating relationships between episodically consumed foods and health outcomes. Biometrics., 65: 1003-1010.

Tooze JA, Midthune D, Dodd KW, Freedman LS, Krebs-Smith SM, Subar AF, Guenther PM, Carroll RJ, Kipnis V (2006). A new statistical method for estimating the usual intake of episodically consumed foods with application to their distribution. J Am Diet Ass. 106: 1575-1587.