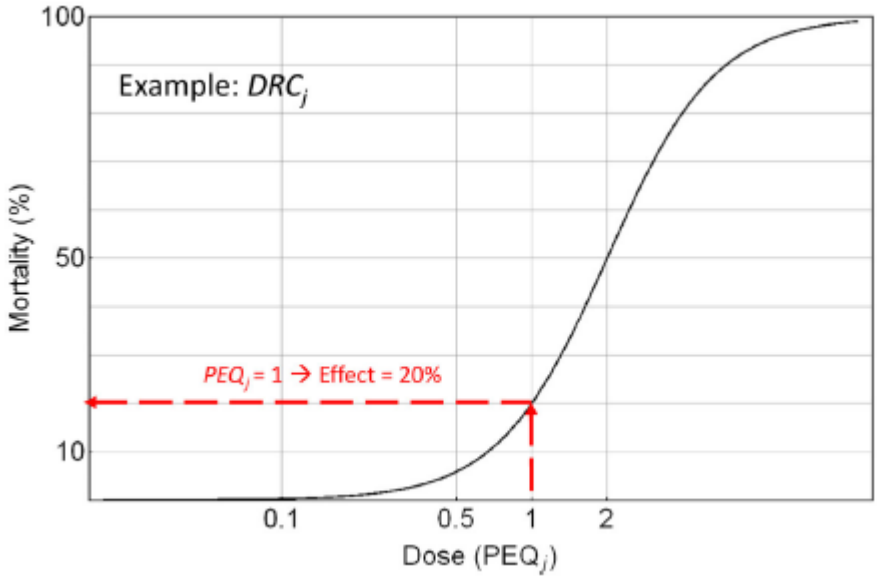
July 2023

How to get a PIE (Predicted individual effect) from a certain Predicted Environmental Quantity (PEQ) (EFSA Bee Guidance Document 2023[1]) using ToxRat.

The new Bee Guidance document from EFSA [2] suggests to use the dose-response model function of a regression to back-calculate the PIE (Predicted Individual Effect) from a certain Predicted Environmental Quantity (PEQ), see Figure from EFSA document, p 67; (DRC = dose response curve):



We are being asked about this more frequently, therefore, we´d like to comment on the possibilities of ToxRat in this context.

Back-calculation of functions for linear regression is not so easy, therefore, users have asked for non linear regression with quantal data in ToxRat.
In ToxRat 4.0, **non-linear regression will also be available for quantal data**. Nevertheless, we are still wondering what the statistical arguments are against the use of linear regression, which is specifically designed for quantal data. Any ideas are warmly welcome!

[1], [2] (Revised guidance on the risk assessment of plant protection products on bees (Apis mellifera, Bombus spp. and solitary bees), EFSA Journal 2023;21(5):7989, 133 pp. https://doi.org/10.2903/j.efsa.2023.7989)

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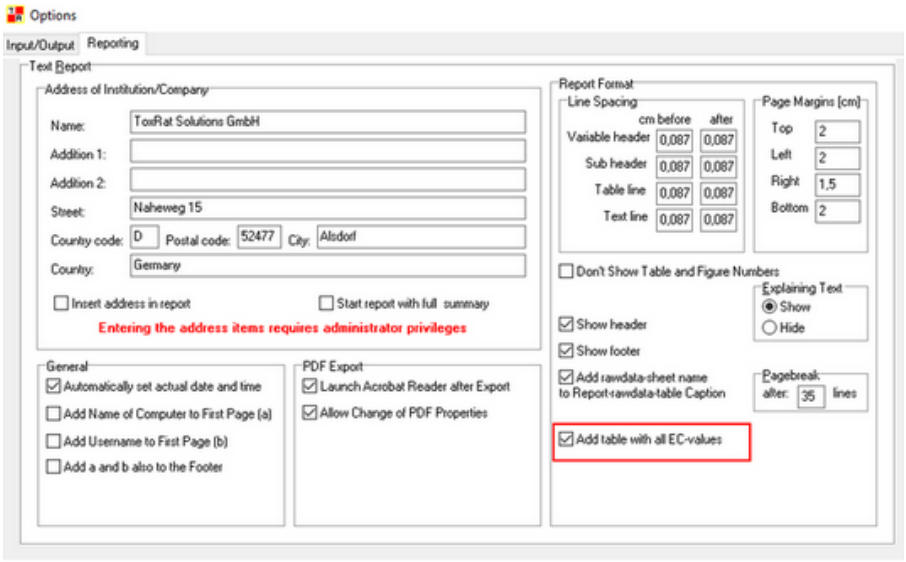
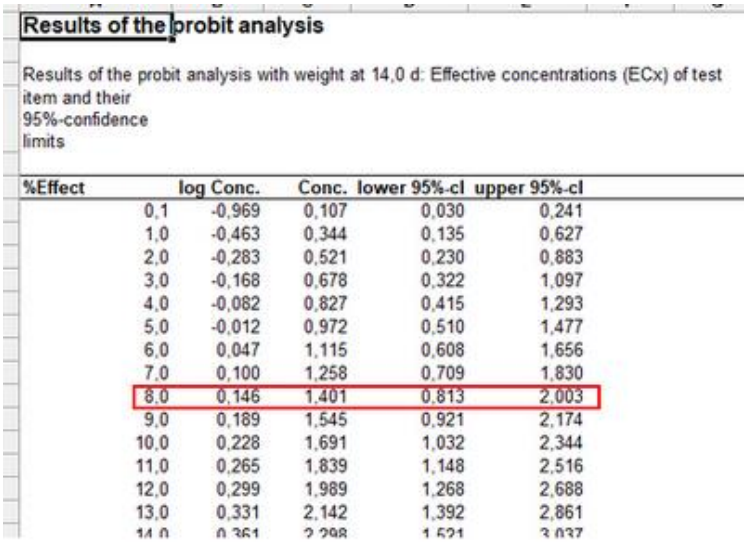
Instead, we would like to point to a feature in ToxRat 330, which allows to get a PIE without back calculations at all and even with a measure for reliability.

- Check the box "Add table with all ECx values":



After a regression was performed, you will find a table with all ECx-values and the confidence limits in 1%-steps (see Menu "Tables" and in the report). This table is nothing else then the basis for the graphics. From menu tables, the results can be copied into an Excel file for further use and to derive a specific PIE:



Results of the probit analysis

Results of the probit analysis with weight at 14,0 d: Effective concentrations (ECx) of test item and their
95%-confidence
limits

%Effect	log Conc.	Conc.	lower 95%-cl	upper 95%-cl
0,1	-0,969	0,107	0,030	0,241
1,0	-0,463	0,344	0,135	0,627
2,0	-0,283	0,521	0,230	0,883
3,0	-0,168	0,678	0,322	1,097
4,0	-0,082	0,827	0,415	1,293
5,0	-0,012	0,972	0,510	1,477
6,0	0,047	1,115	0,608	1,656
7,0	0,100	1,258	0,709	1,830
8,0	0,146	1,401	0,813	2,003
9,0	0,189	1,545	0,921	2,174
10,0	0,228	1,691	1,032	2,344
11,0	0,265	1,839	1,148	2,516
12,0	0,299	1,989	1,268	2,688
13,0	0,331	2,142	1,392	2,861
14,0	0,361	2,298	1,521	3,037

Moreover, there is a general advantage of this procedure compared to back-calculating a PIE for a given predicted environmental quantity (PEQ) from model functions:

In fact, a given %effect calculated from a regression function is not related to a single effect concentration, but to a concentration range defined by lower and upper 95% confidence limits. The confidence limits can be used as reliability criteria for ECx.
However, if you calculate the PIE by back-transforming the regression function, you'll get a single %effect without any information about its reliability.
Instead, back calculating a % effect from a single effect concentration will result in a single "predicted individual effect" (PIE), which **completely lacks any measures of reliability.**

In contrast, if you use ToxRat's function to generate full ECx tables between 1% and 100% effect, you will also get the corresponding confidence limits for ECx, i.e. a range for the relevant effect concentrations. From that, one can derive a range for the corresponding PIE.

For example:
If the relevant PEQ is 1.4 mg/L, then the table shown above will give a PIE of 8%.
It can also be deduced that this 8% PIE is associated with a concentration between 0.813 and 2.003 mg/L (confidence limits of the ECx).
Of course, this does not equate to a "confidence interval" for the PIE. But it can at least give a rough idea of the reliability of the underlying model from which it was derived.
For example, one could also derive the PIEs for the upper and lower CIs of 1.4 mg/L:
0.813 mg/L --> 4% effect
2,003 mg/L --> 12% effect
So, this procedure can be used to derive ranges for the PIE.

Any software that provides regressions and resulting graphs will have the full ECx list including confidence limits, so there should be no problem using it.

We would be happy to discuss about this option, any feedback is welcome!

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