

15, October 2021

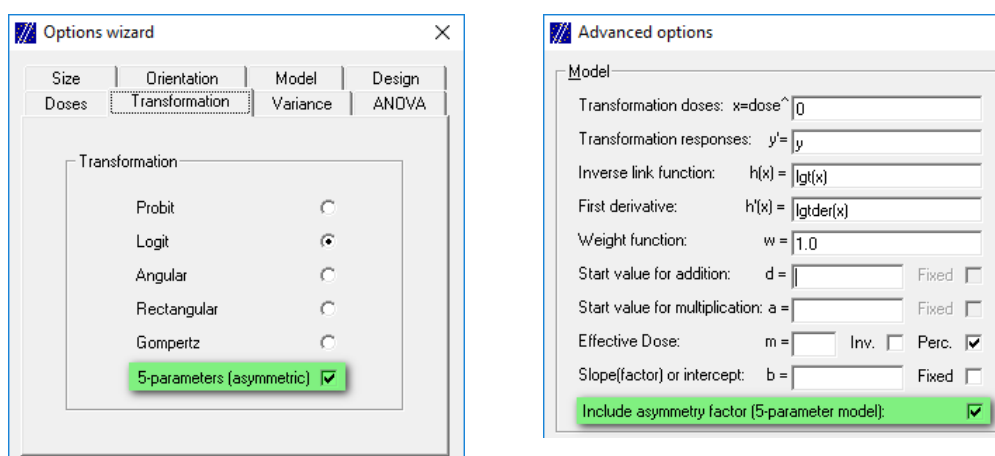
NOTE FOR THE ATTENTION OF: COMBISTATS USERS

Subject: Erroneous calculations in 5-parameter logistic models solved in CombiStats 7.0

There are two ways to select the 5-parameter logistic model (5-PL) in CombiStats:

- Option wizard > 5-parameters (asymmetric), or
- Advanced options > Include asymmetry factor (5-parameter model).

The corresponding windows are given below.



Calculation errors were detected in the case of 5-PL models in CombiStats 6.0 and 6.1.
These errors do not affect the other regression models.

1. Incorrect effective dose values (EDxx)

Effective doses (EDxx) appear in summary tables, below potency results (see next table). They are not reported by default, only upon user's request (advanced options window > Effective dose).

Sample 1			
(IU/ml)	Lower limit	Estimate	Upper limit
Potency	0.556676	0.583385	0.611391
Rel. to Ass.	92.8%	97.2%	101.9%
Rel. to Est.	95.4%	100.0%	104.8%
ED50/ml	131.226	135.677	140.313

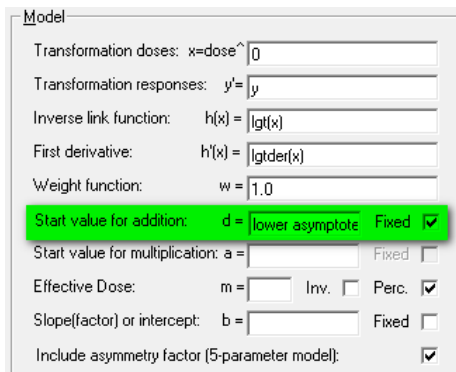
These incorrect effective doses DO NOT affect the potency results.

Therefore, users are kindly asked to follow this recommendation:

DO NOT display effective doses for 5-parameter logistic models in CombiStats 6.0 or 6.1.

2. Fixed d-value (lower asymptote) not supported

Users can define a fixed value for parameter “d” (corresponding to a fixed lower asymptote). The next window shows how to set “d” to a given value (available from Advanced options only).



Model
 Transformation doses: $x = \text{dose}^0$
 Transformation responses: $y = y$
 Inverse link function: $h(x) = \text{lg}(x)$
 First derivative: $h'(x) = \text{lg}(\text{der}(x))$
 Weight function: $w = 1.0$
Start value for addition: $d = \text{lower asymptote}$ Fixed
 Start value for multiplication: $a =$ Fixed
 Effective Dose: $m =$ Inv. Perc.
 Slope(factor) or intercept: $b =$ Fixed
 Include asymmetry factor (5-parameter model):

CombiStats does not apply the fixed lower asymptote in the regression correctly. This leads to a regression model and reported results, including potency estimates, different from that users could expect if the fixed d-value was supported.

Therefore, users are kindly asked to follow this recommendation:

DO NOT set a fixed value for parameter “d” in 5-parameter logistic models in CombiStats 6.0 or 6.1.

CombiStats 7.0

The EDQM has developed a new CombiStats version, which solves the calculation errors above mentioned. Licenced users will receive an email with the link to download CombiStats 7.0.

Important notes.

- Do not forget to uninstall your current version of the software prior to install CombiStats 7.0.
- The credentials of versions 6.0 and 6.1 remain valid and can be used to activate CombiStats 7.0.

The EDQM would like to apology for any inconvenience that these calculation errors may have caused. Would you have any remark or need for further clarifications, please send us a message using the [Helpdesk](#) platform.