



Substance	Tetanus vaccine (adsorbed)
Method	Test in guinea-pigs

Example to illustrate how optimisation by the method of minimum chi-square can be performed with CombiStats. Note that the recommended method of the European Pharmacopoeia is optimisation by Maximum Likelihood: $w=n/(m*(1-m))$ which is the default method if the options wizard is used.

Standard	
Id.	Ph. Eur. BRP1
Ass. pot.	250 IU/amp
Recons.	1 amp / 2 mL
Pre-dil. 2	2 mL / 32 mL
Doses	(1)
1/1	11/12
1/2	8/12
1/4	3/12
1/8	1/12

Sample 1	
Id.	Batch G55K
Ass. pot.	? IU/mL
Convers.	1 mL / 1000 µL
Pre-dil. 2	800 µL / 49.8 mL
Doses	(1)
1/1	12/12
1/2	7/12
1/4	2/12
1/8	0/12

Model: $r/n=(\phi(x))$ where $x=c.+b*\ln(\text{dose})$

Design: Completely randomised

Weight function: $w=n*((1-y)^m+y*(1-m))/(m*(1-m))^2$

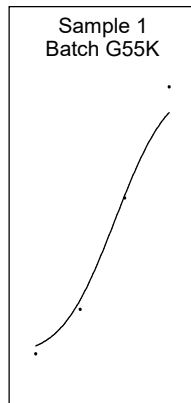
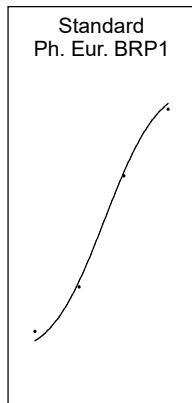
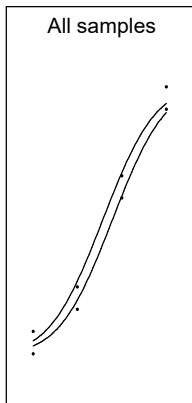
Theoretical variance: 1

Common slope(factor): $b = 1.54266$ (1.23247 to 1.85285)

Correlation | r |: 0.976963 (Weighted)

Source of variation	Degrees of freedom	Sum of squares	Mean square	Chi-square	Probability
Preparations	1	0.0645780	0.0645780	0.0645780	0.799
Regression	1	66.9162	66.9162	66.9162	0.000 (***)
Non-parallelism	1	2.33155	2.33155	2.33155	0.127
Non-linearity	4	0.864549	0.216137	0.864549	0.930
Standard	2	0.456516	0.228258	0.456516	0.796
Sample 1	2	0.408033	0.204016	0.408033	0.815
Treatments	7	70.1769	10.0253	70.1769	0.000 (***)
Theoretical variance			1.00000		
Total	7	70.1769	10.0253		

Sample 1			
Id.	Batch G55K		
(IU/mL)	Lower limit	Estimate	Upper limit
Potency	306.973	418.241	567.166
Rel. to Ass.	?	?	?
Rel. to Est.	73.4%	100.0%	135.6%



Executed by:

Calculated by:

Approved by: