

Attachment 4b:Logarithmic evaluation of EC1.5 values to quantitatively compare WLR

		Log 2 (EC1.5)				AVG Geometric standard deviation		1.61
						AVG Geometric std. dev. without MCI		1.38
SENSITIZERS		rep1	rep2	rep3	rep4			
GIV_hist	Hexyl cinnamic aldehyde	4.2	4.0			Avg Log	4.2 Stdev Log	0.1
GIV_RS				4.3		Avg retransformed	17.9 Geometric std. dev.	1.1
GIV_hist	Citral	4.7	4.4			Avg Log	4.3 Stdev Log	0.3
GIV_RS		3.9	4.3	4.1		Avg retransformed	19.3 Geometric std. dev.	1.2
GIV_hist	Ethylene glycol dimethacrylate	5.6	6.1			Avg Log	6.1 Stdev Log	0.4
GIV_RS		6.1	6.6	6.3		Avg retransformed	70.4 Geometric std. dev.	1.3
GIV_hist	2,4-Dinitrochlorobenzene	1.5	1.1			Avg Log	1.6 Stdev Log	0.4
GIV_RS		1.9	1.3	1.9		Avg retransformed	2.9 Geometric std. dev.	1.3
GIV_hist	4-Methylaminophenol sulphate (METOL)	1.6	1.1			Avg Log	2.4 Stdev Log	1.1
GIV_RS		2.6	2.9	3.9		Avg retransformed	5.3 Geometric std. dev.	2.1
GIV_hist	(5-chloro)-Methylisothiazolinone	-1.2	-0.7			Avg Log	1.4 Stdev Log	2.3
GIV_RS		3.3	1.8	3.7		Avg retransformed	2.6 Geometric std. dev.	4.8
GIV_hist	Phenyl benzoate	<i>not positive in the test</i>						
GIV_hist	Imidazolidinyl urea	6.0		5.4	5.0	Avg Log	5.5 Stdev Log	0.3
GIV_RS		5.6	5.6			Avg retransformed	46.2 Geometric std. dev.	1.3
GIV_hist	Oxazolone	7.4	6.8	7.9	5.5	Avg Log	7.2 Stdev Log	0.8
GIV_RS		7.6	7.6	7.5		Avg retransformed	146.3 Geometric std. dev.	1.8
GIV_hist	4-Phenylenediamine	2.7	1.8			Avg Log	2.9 Stdev Log	0.7
GIV_RS		3.1	3.3	3.5		Avg retransformed	7.4 Geometric std. dev.	1.6
GIV_hist	Cinnamic aldehyde	4.2	3.9	3.9	3.8	Avg Log	3.9 Stdev Log	0.2
GIV_RS		4.0	3.7	3.8		Avg retransformed	14.8 Geometric std. dev.	1.1
GIV_hist	Isoeugenol	3.9	4.3	3.8	3.8	Avg Log	4.1 Stdev Log	0.4
GIV_RS		3.6	4.9	4.1		Avg retransformed	16.9 Geometric std. dev.	1.3
GIV_hist	tetramethylthiuramdisulfide	<i>No statistical assessment made, as some values < 0.98</i>						
GIV_hist	2-Mercaptobenzothiazole	6.1	5.2	5.2	5.7	Avg Log	5.5 Stdev Log	0.3
GIV_RS		5.1	5.7	5.6		Avg retransformed	45.6 Geometric std. dev.	1.3
GIV_hist	Eugenol	<i>not positive in the test</i>						
GIV_hist	Cinnamyl alcohol	6.4	7.6	7.3	5.9	Avg Log	6.8 Stdev Log	0.6
GIV_RS		6.8	6.9	6.4		Avg retransformed	108.4 Geometric std. dev.	1.5
GIV_hist	Glyoxal	6.5	6.5	6.4	6.5	Avg Log	6.7 Stdev Log	0.3
GIV_RS		7.0	7.0	7.1		Avg retransformed	106.2 Geometric std. dev.	1.2
GIV_hist	4-nitrobenzylbromide	0.1	0.7			Avg Log	0.4 Stdev Log	0.4
GIV_RS		0.3	0.2	1.0		Avg retransformed	1.4 Geometric std. dev.	1.3
GIV_hist	Methyldibromo glutaronitrile	3.3	2.5			Avg Log	3.3 Stdev Log	0.6
GIV_RS		4.0	3.1	3.8		Avg retransformed	10.1 Geometric std. dev.	1.5

Explanations

All logarithmic values were calculated with the base 2, this is more intuitive as compared to base 10 since two-fold logarithmic dilution steps were always pipetted; thus the logarithmic value correlates to the number of wells in the plate to reach EC1.5

Avg Log the average of the logarithmically transformed values

Avg retransformed the retransformed logarithmic average or geometrical mean, ($=2^{\text{Avg Log}}$); in our study in most cases close to the arithmetic average

Stdev Log the standard deviation of the logarithmically transformed values

Geometric standard deviation

This corresponds to a factor, thus we can describe the experimental variation as:

EC1.5 = geometric mean * / geometric Stdev

instead of

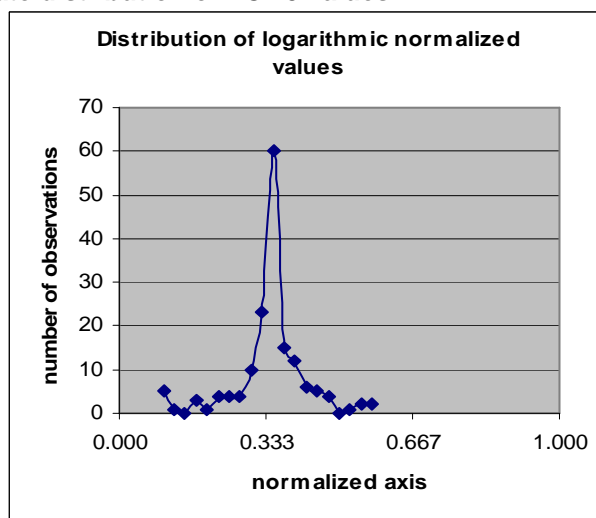
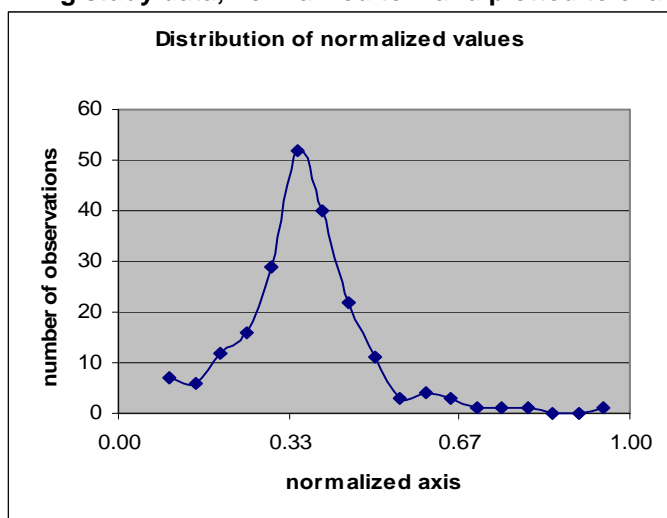
EC1.5 = arithmetic average \pm STDEV

Numerical example: If the standard deviation of the Log2 transformed values is 0.5, the geometric standard deviation is 1.414 or the square root of 2. The 95.4% confidence interval of the Log2 transformed values then becomes ± 1 (i.e. twice the standard deviation) and the geometric (or re-transformed) 95.4% confidence interval is confined by a factor of 2. Thus in this specific case, the 95.4% confidence interval is covered by the concentration range one well in the microtiter plate up and down of the geometric mean.

There are two reasons for this approach:

- The data overall are closer to a Log-normal distribution (see below graphs), and therefore logarithmic calculations better describe the data
- these retransformed logarithmic standard deviation are scale-independent and can be compared between different chemicals with differing potency

All ring study data, normalized to 1 and plotted to evaluate distribution of EC1.5 values



Slightly skewed distribution of normal values (left) and symmetrical distribution of log transformed values (right)