Appendix F
Decimal Geometric Concentration Series

Note: Whereas geometric concentration series (as opposed to arithmetic concentration series) are regarded as a requirement in for any cytotoxicity assay that is based on concentration response analysis, the decimal geometric concentration series described below is just a recommendation.

In general **dose-response relationships** of many pharmacological or toxicological endpoints investigated have a **nonlinear**, often sigmoidal shape, which can be linearized to some extent by logarithmic transformation of the x-axis. This usually has to be done when IC_{50} values are calculated either by regression analysis or by graphical estimation for the current NRU assay.
If the concentration series is done with arithmetic progression steps, transformation of the x-axis will result in an unequal distribution of measurements. Therefore, the use of a geometric concentration series (= constant dilution / progression factor) is recommended. The simplest geometric series are **dual geometric series**, e.g., a factor of 2. These series have the disadvantage of numerical values that permanently change between logs of the series (e.g., *log0*-2, 4, 8; *log1*- 16, 32, 64; *log2*- 128, 256, 512; *log3*- 1024, 2048,).

The **decimal geometric series**, first described by Hackenberg and Bartling (1959) for use in toxicological and pharmacological studies has the advantage that independent experiments with wide or narrow dose factors can be easily compared because they share identical concentrations. Furthermore, under certain circumstances, experiments can even be merged together:

EXAMPLE:

10						**31.6**						**100**
10				**21.5**				**46.4**				**100**
10		**14.7**		**21.5**		**31.6**		**46.4**		**68.1**		**100**
10	**12.1**	**14.7**	**17.8**	**21.5**	**26.1**	**31.6**	**38.3**	**46.4**	**56.2**	**68.1**	**82.5**	**100**

The dosing factor of **3.16** (= $\sqrt[2]{10}$) divides a log into 2 equidistant steps, a factor of **2.15** (= $\sqrt[3]{10}$) divides a decade into 3 steps. The factor of **1.47** (= $\sqrt[6]{10}$) divides a log into 6 equidistant steps, and the factor of **1.21** (= $\sqrt[12]{10}$) divides the log into 12 steps.

For an easier biometrical evaluation of several related concentration response experiments use decimal geometric concentration series rather than dual geometric series. The technical production of decimal geometric concentration series is simple. An example is given for factor 1.47:

Dilute 1 volume of the highest concentration by adding 0.47 volumes of diluent. After equilibration dilute 1 volume of this solution by adding 0.47 volumes of diluent...(etc.).

Reference:

Hackenberg, U. and H. Bartling. 1959. Messen und Rechnen im pharmakologischen Laboratorium mit einem speziellen Zahlensystem (WL24-System). Arch. Exp. Pathol. Pharmakol. 235: 437-463.