

# Dobrodošli!

# Design and Evaluation of BE Studies

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# Answering the Question: What is Enlightenment?

„Enlightenment is man's emergence from his self-imposed immaturity for which he himself was responsible. Immaturity and dependence are the inability to use one's own intellect without the direction of another. **One is responsible** for this immaturity and dependence, if its cause is not a lack of intelligence, but a lack of determination and courage to think without the direction of another. **Sapere aude!** Have courage to use your **own** understanding! is therefore the slogan of Enlightenment.”

Beantwortung der Frage: Was ist Aufklärung?

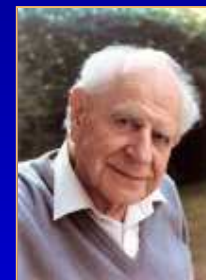
„Aufklärung ist der Ausgang des Menschen aus seiner selbst verschuldeten Unmündigkeit. Unmündigkeit ist das Unvermögen, sich seines Verstandes ohne Leitung eines andern zu bedienen. Selbst verschuldet ist diese Unmündigkeit, wenn die Ursache derselben nicht am Mangel des Verstandes, sondern der Entschließung und des Muthes liegt, sich seiner ohne Leitung eines andern zu bedienen. Sapere aude! Habe Muth, dich deines eigenen Verstandes zu bedienen! ist also der Wahlspruch der Aufklärung.

*Immanuel Kant (1784)*

# To bear in Remembrance...

Whenever a theory appears to you as the only possible one, take this as a sign that you have neither understood the theory nor the problem which it was intended to solve.

*Karl R. Popper*



Even though it's *applied* science we're dealin' with, it still is – *science!*

*Leslie Z. Benet*



# Main Topics

- Bioequivalence
  - Surrogate of clinical equivalence or
  - Measure of pharmaceutical quality?
- Types of studies
  - Pharmacokinetic (PK)
  - Pharmacodynamic (PD)
  - Clinical (equivalence and/or safety/efficacy)

# Main Topics

- Types of studies (cont'd)
  - Healthy Subjects
  - Patients
  - Single dose
  - Multiple dose
  - Cross-over
  - Parallel
  - Reference product (another modified release formulation, IR, solution)

# Main Topics

- Types of studies (cont'd)
  - (PK interaction)
  - Food effect
- Design Issues
  - Dose regimen
  - Fasted / fed state
  - Type of standard meals
- Bioanalytics (*not* GLP!)
  - Parent drug / metabolite(s) / enantiomers / pro-drugs
  - Validation / routine application

# Main Topics

- Ethics (GCP!)
  - Dose levels / number of administered doses
  - Number / volume of blood samples
  - Drug and/or adverse effects
- Clinical performance (GCP!)
  - CRO selection
  - Responsibilities of sponsor / investigator
  - Audits / monitoring

# Main Topics

- **NCA / PK (PD)**
  - Sampling schedule
  - Metrics (AUC,  $C_{max}$ ; AUEC,  $Ae_{max}$ , ...)
  - Design, methods, evaluation
- **Sample size**
  - Estimation from previous and/or pilot studies, literature
  - Highly variable drugs
- **Biostatistics**
  - Models & assumptions
  - Protocol, evaluation, report



# Main Topics

- 'What if'-scenarios
  - Common pitfalls
  - Problems in clinical performance – studies 'on hold'
  - Failure to meet the required performance in bioanalytics
  - Blind review
  - 'Failed' studies
  - Deficiency letters

# Another reminder

**Rose  
is a rose  
is a rose  
is a rose.**



***Gertrude Stein (1913)***

**Guidelines  
are guidelines  
are guidelines.**

***Henrike Potthast (ca. 2004)***

**In advanced engineering, you expected failure; you learned as much from failures as from successes – indeed if you never suffered a failure you probably weren't pushing the envelope ambitiously enough.**

***Stephen Baxter; Transcendent, Chapter 36 (2006)***