From courses to careers: A Pharmaceutical perspective

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Specific Opportunities

- Preclinical – Discovery
- PDM
- Toxicology
- Pharmaceutical Sciences
- Drug manufacturing
  - A series of funnels or filters

- Apply Statistical methods to help drive decisions
Early Discovery

- Find something that does something..
- Target: scientific literature, market research
- High Throughput Screening / Discovery Biology
  - DOE for Assay Design
  - Control Charting
  - Exploratory Data Analysis
  - Non-linear Dose Response Models
  - Multiple Comparisons
  - Structure Activity Relationship (PLS, SVM, etc)
- How do we modify a molecule that is “close”?
- How do we select which compounds will continue?
Dose Response / Non Linear Model
- Variance – constant, proportional?
- Transform: $x^?, y^?$ both?

Data fitting or coefficients with intrinsic meaning?
- Rate of binding
  - Coefficients may tell the scientists what mechanism(s) are at work

2x2 table but 99%+ in one cell?
PDM (Pharmacokinetics, Dynamics and Metabolism)

- What the drug does to the body
- What the body does to the drug
- More in-depth information on fewer compounds.
- Dose response:
  - \( T_{\text{max}}, C_{\text{max}}, \text{AUC}, \text{half-life} \)
  - Non-linear modeling
- Battery of safety assays
- How do we “build” and assess the assays?
- How do we select which compounds continue?
- Is the “best” good enough?
- Do in-vitro (lab) and in-vivo (animal) data:
  - Correlate?
  - Substitute?
How does the drug perform in animal studies?
- Is there a dose response?
- Is there a safety window?
- Are any systems negatively impacted?
  - Kidney, liver, brain, body weight, heart function?
- Are the offspring impacted? (Thalidomide)
- Limited “n” (want to “prove” no Adverse Events)

One study may “kill” a compound

ANOVA, Dose trending, multiple comparisons

Reporting, validation and documentation much more stringent compared to early discovery
Pharmaceutical Development

- If a compound works, how can we make it?
  - Chemical synthesis (DOE, EDA)
  - Biological process – grow cells, clean cells (DOE)

- How can we test it? (Analytical methods)
  - Method development
  - Method precision, linearity, bias, robustness
  - Do we have uniformity in our tablets and capsules?
  - Does our delayed release formulation work as intended?

- How can we preserve its functionality over time?
  - Formulation (DOE, Mixture Experiments)
  - Stability Testing (Regression, ANCOVA)

- Overall, do all three pieces above have a robust, controlled process? (Quality by Design)
  - Lab → Pilot → Commercial scale (DOE, modeling)
  - Testing to support label claims, product performance over time
Global Supply (Manufacturing)

- Process Control, process capability
- Investigational work, annual reviews
- What process variables are contributing to process variation?
- Changes: facility, supplier, method, reagent
- Can we improve our process: time, $$, greener?
  - DOE
  - Total Quality Management / Six Sigma