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?

Early Discovery

- 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:
  - Tmax, Cmax, AUC, 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?

Safety / Toxicology

- 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