

# Application of Statistics in Global Research at Novo Nordisk

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## Novo Nordisk at a glance

Novo Nordisk is a global healthcare company with 90 years of innovation and leadership within:

- diabetes care
- insulin
- injection devices
- More than 40,000 employees around the world
- Biostatistics departments ~ 200 statisticians in Development



## Global Research

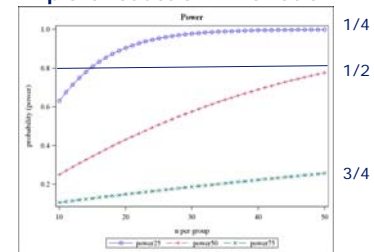
- Discovery and validation of clinical proof of principle of new analogues and/or formulations
- 1,500 employees



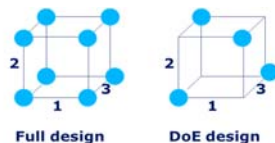
## Design of experiments

- Sufficient number of animals in studies
- Power & sample size calculations

Explore reduction in variation



## Design of experiments cont'



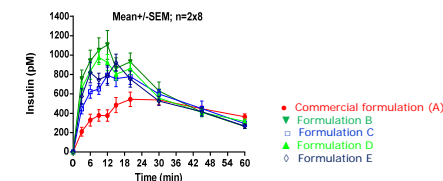
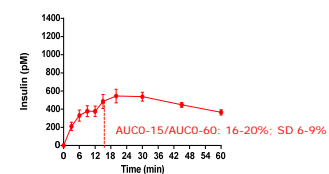
With DoE: The selected experiments produce maximum amount of relevant information

- Analogue DoE
- Full design: 72 analogues
- DoE approach: 18 analogues
- Formulation DoE
- Full design: 54 formulations
- DoE approach: 15 formulations



## Statistical analysis – an example

Faster absorption of insulins



- Required sample size (SD 7%):  
5% difference in means: 31  
7% difference in means: 16

Formulation	Tmax' (min)	AUC(0-15/0-60) (%)
A	30	17
B	9	34**
C	15	27**
D	12	32**
E	15	31**

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'Median,  
\*\*p<0.0001; Pairwise comparisons to formulation A



## Multivariate statistics

- PhD projects:
- *In silico* ADME Classification of Drug Candidates, 2003-2006

Table 1. Calculated Molecular Descriptors and Experimental Apparent Permeability,  $P_{app}$ , Values for Compounds in the Calibration Data Set<sup>a</sup>

descriptor	class 0 (380 compounds)		class 1 (332 compounds)		total (712 compounds)	
	mean	std. dev.	mean	std. dev.	mean	std. dev.
clogP	4	2.2	3	1.2	4	1.8
ROT	11	4.0	8	2.4	9	3.7
HA	8	2.2	6	2.1	7	2.4
HD	3	1.2	1	1.1	2	1.4
mlogP	3	1.2	3	1.1	3	1.2
SURF	567	142	447	74	511	130
VOL	551	146	425	78	492	135
MW	492	117	373	78	437	117
PSA	107	35	65	28	87	38
$P_{app}$	0.5	1.0	33	25	16	24

Table 6. Classification of 112 External Compounds from Five Nearest Neighbors in the Calibration Data Set<sup>a</sup>

	predicted class 0	predicted class 1	not predicted	sum
lab test class 0	53	16	4	73
lab test class 1	0	35	4	39
sum	53	51	8	112

<sup>a</sup> Permeability class: (0)  $P_{app}$  below  $4 \times 10^{-6}$  cm/s and (1)  $P_{app}$  on  $4 \times 10^{-6}$  cm/s or higher.

Refsgaard et al 2005 J Med Chem 48: 805-811

- Characterization of absorption enhancers for orally administered therapeutic peptides in tablet formulations – applying statistical learning, 2013-present

