Clinical studies

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aCROnordic

- **Spadille** established in 1971
  - First CRO in Scandinavia
- **aCROnordic** established in 2003
  - Merger of Spadille ApS, Spadille Clinical Trials ApS and **MediMentum** ApS
  - No. 1 - Clinical CRO in Denmark
- Goal to become the first **Nordic Development CRO**
- HQ in DTU Science Park in Hørsholm
- Staff of 60 people

Our clients

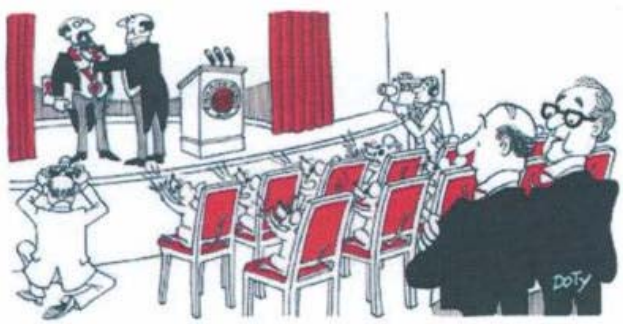
Agenda

- Short introduction to clinical studies
- Challenges in clinical development

Why do clinical studies?

- Clinical studies are studies in humans designed to establish safety and efficacy of interventions

Why do clinical studies?



"It's an award for a cancer cure, but it only works on mice."

Why do clinical studies?

- Double blind RCT the ultimate proof of efficacy
  - HDL cholesterol-Torcetrapib
- Double blind RCT no guarantee for safety
  - Troglitazone, Vioxx, Exanta
- Why have so few functional food compounds been tested?

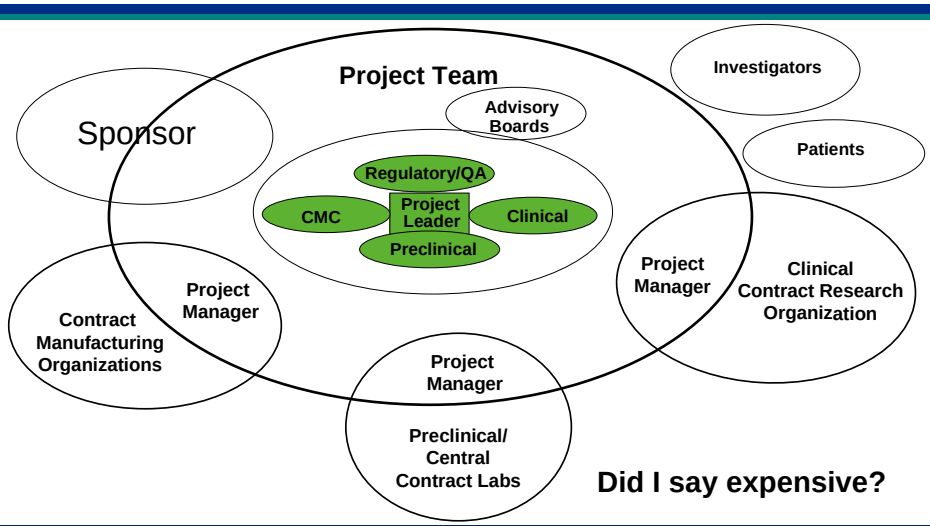
Ethical considerations

- Sufficient non-clinical data needed
- Approval from Ethical Committees/IRBs needed
- Declaration of Helsinki - protects the rights of subjects
- Good Clinical Practice – rights, safety, credible data
- Placebo
- …….

Phases in clinical development

Phase	Time	What
I	1 y	Safety, PK/PD in HV
II	1-2 y	Terapeutic explorative
III	2-3 y	Terapeutic confirmatory

Matrix for a clinical study



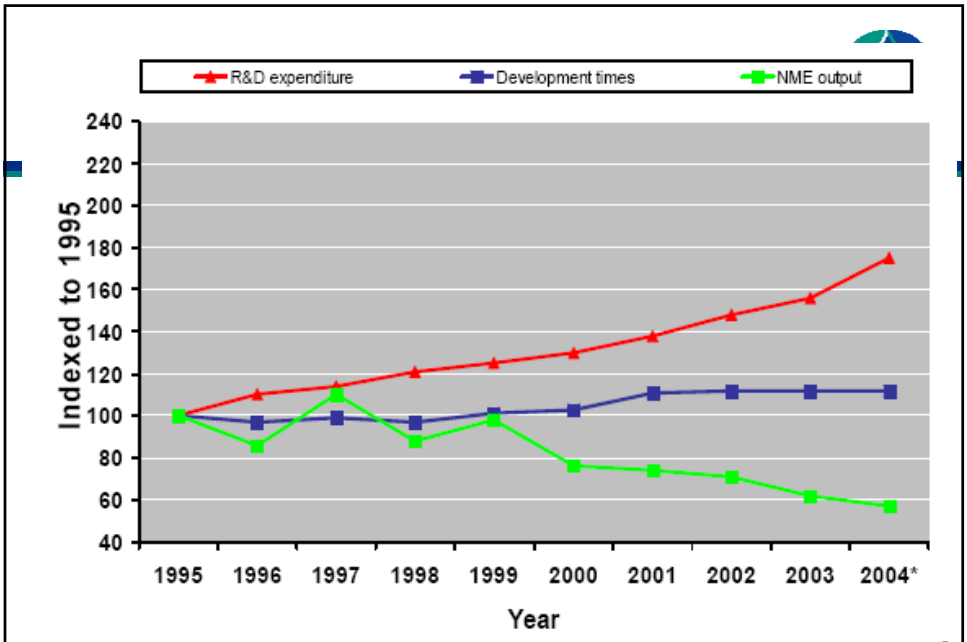
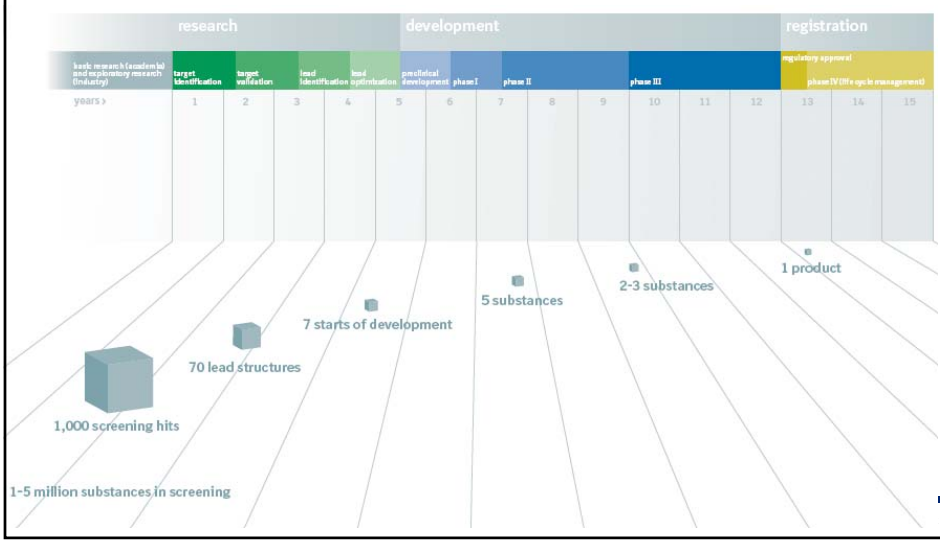
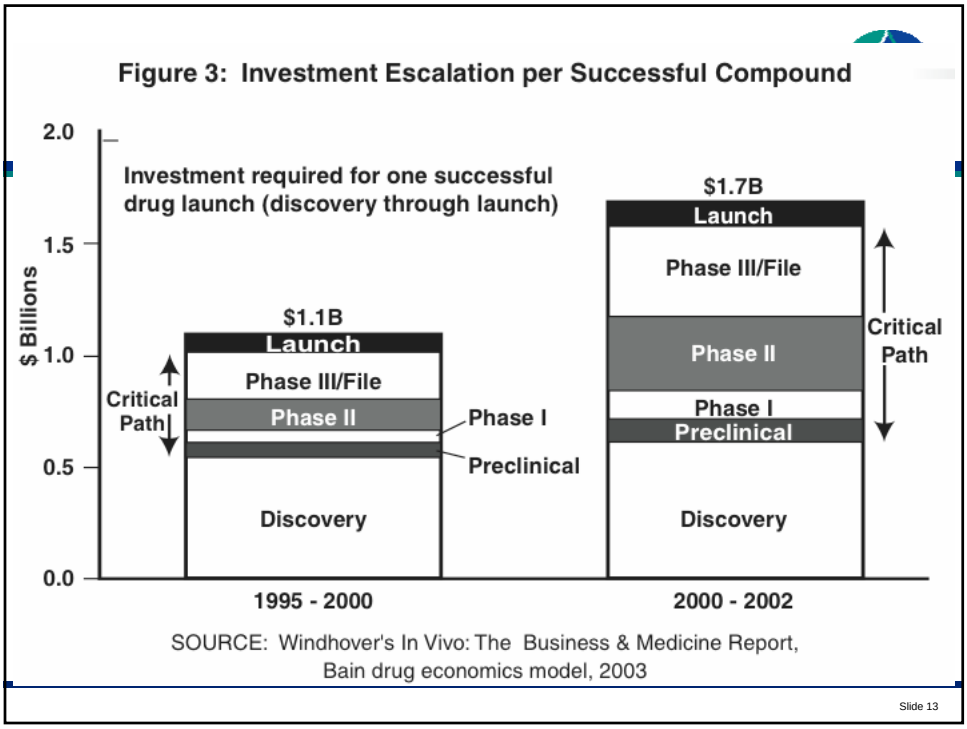


Figure 3 : Global R&D Expenditure, Development Times and NMEs 1995–2004[5]

Slide 11

High attrition rates





Biomarkers

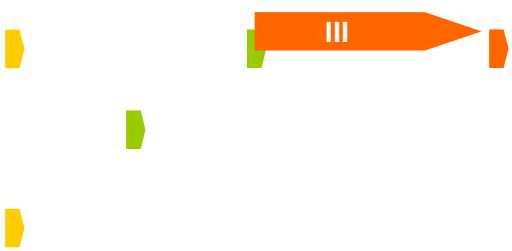
- Measurable characteristics reflecting disease processes
  - Circulating molecules (HbA1c, Cholesterol….)
  - Biopsies (proteins, RNA….)
  - Physiological measures (BP….)
  - Genetic testing (CYP….)
  - Imaging (DEXA, PET….)
- If the biomarker predicts clinical outcome
  - **surrogate endpoint** or **personalized medicine**

Innovative study designs

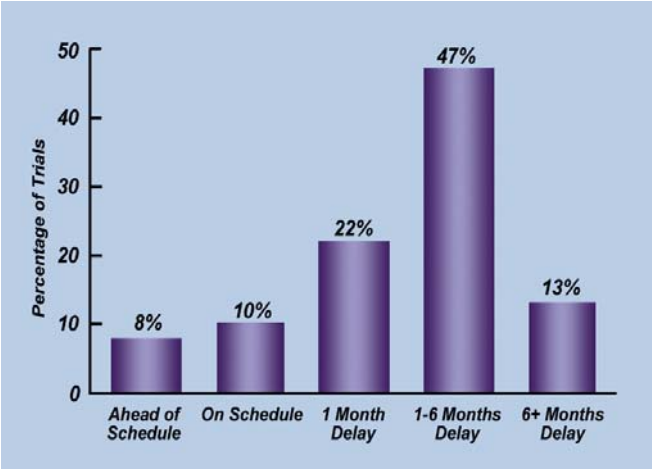
- Adaptive study design
  - Thorough planning pivotal
  - Statistical expertise needed
  - Regulatory risk
- Concentration-controlled…..
- Validated composite endpoints

- May reduce
  - Need for patients
  - Time to market

Phase and go



Patient recruitment delay trials



>50% time used in clinical trials

Recruitment phase ~ 1 year (1/3 of total time)

Source: CenterWatch 1998.

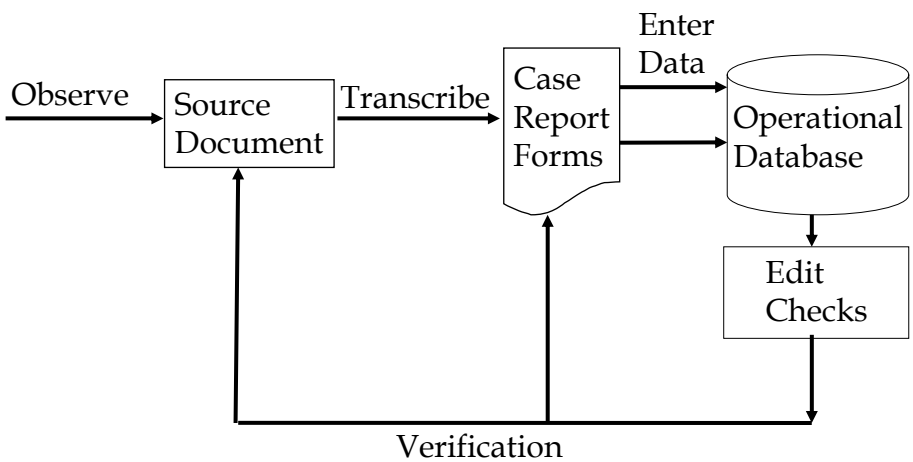
Keys to successful recruitment

- Broaden the population
- Access to
  - Patient databases
  - Investigator networks / SMO's
- Do a thorough feasibility
- Use the GP and media (newspapers, facebook,…)
- Spend time on your patient directed communication

Data management

- Data volume is enormous
- Data collected and stored in different systems and formats
- Need for fast decision making based on data
- Formats are important
  - Integrated safety database
  - Data mining across studies
- Standards minimize errors and maximize efficiency
  - CDISC

Classical Data Handling

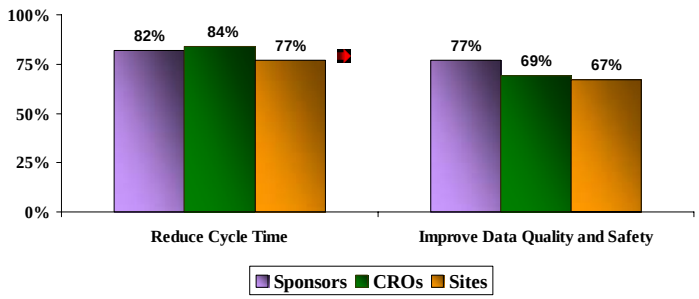


We know the potential of EDC….

"EDC is a Major Strategic Initiative that will…"

Percent Agree

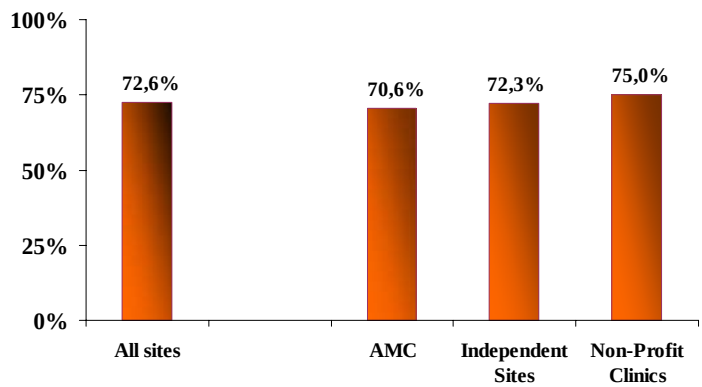
Source: CDISC-CenterWatch, 2002



Respondents, n=750, Pharma companies, n=211, Sites n=355, CROs, n=146

…but we don't use it!

Percent of Investigative Sites



Source: CDISC-CenterWatch, 2003

Geography

- Regions differ with respect to
  - Recruitment potential
  - Cost
- Consider
  - Time to get study approved
  - Import/export barriers
  - Cost of courier transport
- Flexibility is key

Conclusions

- Clinical studies are essential for new treatments
- Early and thorough planning is key
- Good clinical programs add value to our company
- Consider alternatives to “me too” programs
  - Biomarkers
  - Innovative study designs
- Ensure operational planning
  - Patient recruitment is key
  - Use Standard Data Formats
  - EDC
  - Ensure geographic flexibility