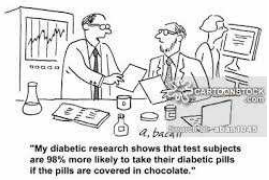
# Feasibility in recruitment: expectations and reality check




Interactive presentation by
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## Disclaimer

This presentation represents a personal view,

but **not** the official company point of view.

Sponsor´s view (Dr. Wolfgang Seibold)

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## Sponsor – basic considerations

- Program:
  - Plan for success: Time, budget, enrichment of patients
  - Integration of external experts in advisory boards
- Protocol:
  - Phase 1/2: maximize chance of success by selecting the right patients
    - Enrichment for e.g. CRP-negative, treatment-naive patients to achieve Proof of Concept
  - Phase 3: harmonization of protocols in the program
    - Eligibility, study procedures, safety
    - Focus on desired label claim and reimbursement discussions
- Recruitment:
  - Recruitment timelines should be ambitious, challenging, and doable
  - Comparison to known internal and external trial data
  - And we have a Site Feasibility Questionnaire ….



## Sponsor - country and site feasibility

- Instrument: site feasibility questionnaire

- Difficulties:
  - Targeted indications are getting more narrow than in the past
  - Study procedures and design are getting more complex
  - Prediction of patient´s willingness to participate in any trial
  - Prediction of competitive situation

- Questions:
  - Which eligibility criteria are reliably coded in a ´typical´ site´s database?
  - What implications does a conservative commitment have for the site? But also for the country manager in a global organization?
  - Are these numbers only a first step in the discussion between sponsor and site?
  - Or should the numbers be adapted by the sponsor for a ´realistic´ planning?

## The value of feasibility questionnaires

Why are recruitment estimates so often incorrect?

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Three different recipients:

- Hospitals / KOL
  - Possible problems: no time/busy staff, no detailed patient database
- Medical practices
  - Possible problems: no detailed patient database, no study nurse
- Clinical Trial Unit / Professional Site
  - Possible problems: too many feasibility questionnaires per month, bias because of detailed experience with feasibility processes

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## The value of feasibility questionnaires

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Feasibility questionnaires tend to get more and more detailed

(1) N° of patients (>18 and <65 years old) with a physician diagnosis of asthma for ≥12 months, based on the GINA 2014 Guidelines ✓ ?

(2) Among (1) N° of patients with existing treatment with medium to high dose ICS (≥250 mcg of fluticasone propionate twice daily or ... ✓ ?

(3) Among (2) N° of patients with prebronchodilator forced expiratory volume (FEV1) 55 to 80% of predicted normal ?

(4) Among (3) N° of patients with documented reversibility from historic data within 1 year of at least 12% and 200 mL in FEV1 after the administration of 200 to 400 mcg albuterol/salbutamol… ✓ ?

(5) Among (4) N° of patients with a fractional exhaled nitric oxide (FeNO) ≥26ppb ??

6 more questions up to N° 11!

**Feasibility questionnaires are often just gut feeling and not as reliable as they seem!**

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## The value of feasibility questionnaires

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Important opportunity to give feedback on Inclusion/Exclusion Criteria
- Small changes can make a big difference:
  - BMI <32 instead of <30
  - Systolic blood pressure below 150 instead of 140

Sponsor/CRO should assess if certain In/Ex are really justified and necessary
- "Wrong reasons" for not being able to change In/Ex:
  - "We have to use our standard template"
  - "It is too difficult to change them at this stage of the project"
- Small companies/biotechs are much more flexible than big pharma

**Listen to the advice of sites!**
**Do not insist on In/Ex just because changing them is difficult!**

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## Sponsor – challenges during preparation

- Timelines:
  - Constant shift in timelines due to various reasons
    - e.g. budget, medication, regulators, operations, contracts
- Clinical Trial Protocol:
  - Constant challenge by internal discussions regarding eligibility criteria, forbidden medications, study procedures, … but also
  - Scientific Advice Meetings, Experts, and Patient Advocacy Groups
  - Regulators: critical, since typically received in the vulnerable and unflexible period during ongoing submissions in a multinational trial

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## Sponsor – challenges during preparation

Discussions on Pre-screenings:

- Study-specific or unspecific?
- Planned reimbursment in the contract?
- Regulatory approvals needed?

Discussions on advertisement:

- Local advertisment as part of standard investigator´s contract
- Sophisticated advertisement techniques
- Involvement of satellite sites or use of referral systems by the site

**How do all these changes and discussions impact the given site feasibility and commitment?**

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## Recruitment tools and advertisement strategies

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- Patient database
  - Most important asset!
  - The more detailed the more useful
  - Needs an administrator and much maintenance
- Advertisements in local newspaper
  - Good tool for special patient populations
  - ~ 5.000€ per advertisement in Hannover
  - Important to include patient remuneration!

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## Recruitment tools and advertisement strategies

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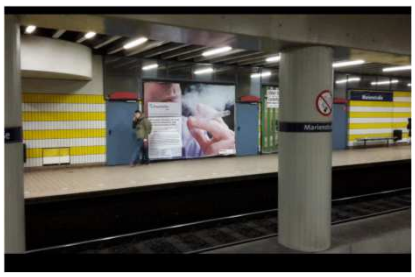
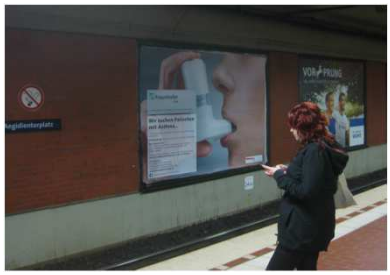
- Advertisements on billboards
  - Same format as in newspapers
  - ~ 3.600€ for 10 days in 16 underground stations





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## Recruitment tools and advertisement strategies

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- Internet campaign
  - Performed by an external provider
  - Advertisements connected to Google searches
  - Advertisements on relevant Web pages
  - Mailings
  - Minimum costs are 2.000€
- Radio advertising
  - Difficult to put across enough information
  - Quite costly (~ 20-200€ per 30-sec spot in a local radio station in Hannover, depending on day and time)

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## Recruitment tools and advertisement strategies

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- Facebook (social media)
  - Great tool for healthy volunteers and relevant patient groups
  - Quite cheap, can be successful with just a few hundred Euros
  - Dedicated staff is needed to look after the account and to answer comments/questions!

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## Recruitment tools and advertisement strategies

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- Referrals from hospitals/medical practices
  - Important for rare patient groups
  - Needs a lot of encouragement
  - Compensation is important (e.g. 100 € per referral)

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## Recruitment tools and advertisement strategies

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### Summary

- Different media for different patient populations
- Costs for advertisements per contact has a large variability
  On average it is 50€ per contact at our site
- Only use Facebook and other social media if you have dedicated staff to look after the account
- To get referrals can be difficult and frustrating

**Advertisements can be extremely useful!**
**Don't be too tight about the budget for advertisement!**

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## Sponsor - challenges during trial conduct

- Ensure operational and medical excellence in all trial functions (staff, vendors, logistics, …)
- Clear and open communication with the sites in a business relationship with trust and empathy but also clear expectations based on given commitment
- Sponsor`s major task:
  - Listen, support, request – and react in a timely manner
  - Identify the need for actions early and act consequently

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## Communication between site and sponsor/CRO

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- Adherence to recruitment estimates is key to a good site reputation
- Recruitment problems should be discussed in an open manner and without hesitation
- Protocol amendments to change In/Ex:
  - Early assessment of recruitment hurdles is important
  - Time and effort spent on amendments can be worthwhile in the long run



## Sponsor – potential actions if recruitment is behind expectations

- Globally:
  - Identification of issues and increase the pressure
  - Adaptation of timelines or sample sizes
  - Addition of new countries and new sites
  - Promotion of the trial: Initiate recruitment campaigns, publications, involve patient advocacy groups, motivate sites
- Locally:
  - Identification of issues and increase the pressure
  - Adaptation of country commitment
  - Adaptation of investigator fees, patient reimbursements
  - Addition of new sites
  - Promotion of the trial…

## Sponsor - Revision of eligibility criteria to support recruitement

- Prerequisites:
  - Identification of one or few eligibility criteria or other protocol-related issues as recruitment hurdles
  - Planned revisions do not change the safety, efficacy or consistency considerations in a substantial manner
    - Fast recruiting, but scientifically invalid trials are a waste of money
- Pro´s:
  - Easy and straightforward solution on 1st view
  - Motivating aspect for sites
- Con´s:
  - Effect is not always as beneficial as expected
  - Regulatory approvals are time intensive and cost intensive



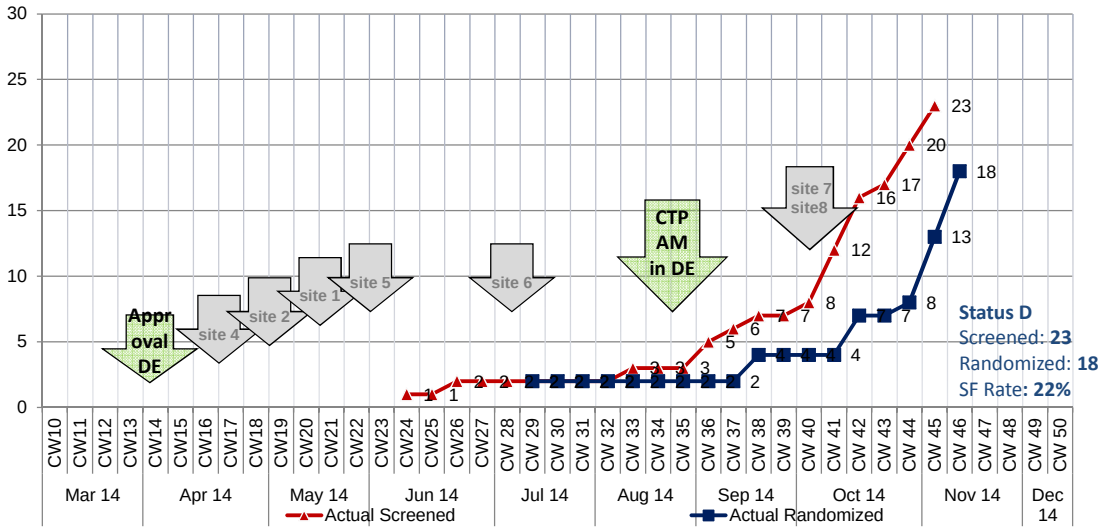
## Sponsor – example 1 in ankylosing spondylitis

Recruitment in Germany

- Enrichment of patients with ongoing inflammation (CRP> ULN) was planned from the beginning and was criticized by investigators from the beginning
- Recruitment rate was slower than expected
- Amendment to allow normal CRP levels was implemented….
- Recruitment improved afterwards, but mainly due to a new site – and 2 of 3 patients were still CRP-positive

# Sponsor – Example 1 in ankylosing spondylitis

## Recruitment in Germany

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# Sponsor – example 2

## Alzheimer´s disease

Recruitment was slower than committed by sites which resulted in need for a protocol revision

1. Reduction of assessments to ease patient burden
2. Allow previous AD medication use & allow previous participation in studies/trials
3. Allow current use of certain AD drug, drop comparison arm

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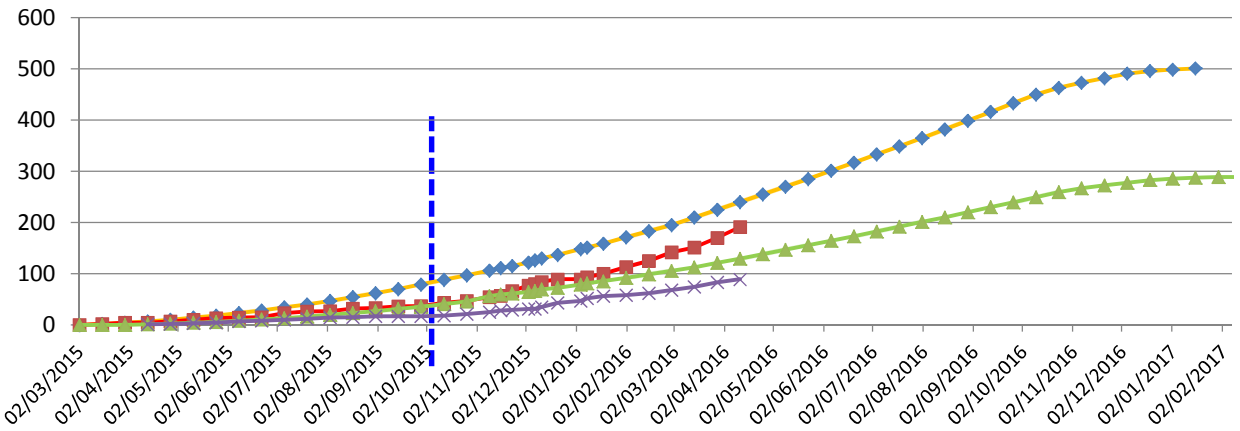
# Sponsor – example 2

## Alzheimer´s disease

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# Sponsor - take home messages

- Ensure your study meets the requirements needed for your drug
- Know the limitations of your feasibility process
- Discuss known or unknown recruitment obstacles with sites
- Take appropriate actions after thorough review of the issue
- Open-minded, personal communication is key

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## Site - Take home messages

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- Feasibility Questionnaires can be very time-consuming to answer
- The more detailed Feasibility Questionnaires are the more unreliable they get
- Be open to discuss and amend In/Ex during the feasibility process
- Advertisement is expensive, gives sites enough budget for it

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