Bästa möjliga data - ny teknik hjälper dig att följa dina kliniska prövningar i realtid

2013-05-30

Sverre Bengtsson, VP Business Development, Co-founder Pharma Consulting Group/PCG Clinical Services
Pharma Consulting Group – PCG

• Full service CRO working globally
• Phase I through IV
• Medical Device studies
• 350 studies in all major indication areas performed since 2003
• Viedoc™ – Web based eCRF, monitoring and project management tool for efficient management of your trials
Recruitment and performance metrics*

• 70 % of clinical trials don’t reach recruitment goal
• Up to 30 % of the sites do not recruit any patients
• Up to 95 % of all delays are caused by slow recruitment
• <5 % of U.S. or EU adults with cancer enter into a clinical trial even though they present opportunities to receive novel treatments for their disease.** ***
• <25 % of screened patients remain in the treatment protocol until a trial ends ****

*Eglmeir, W, Head Clinical Operations at Grüenthal, presented at DIA Clinical Forum 2010
** AACR 2011 Annual Report, Page 65
**** “Drug Developers Actively Improving Efficiency Of Clinical Trials” Tufts Press Release April 26, 2011
Recruitment and performance metrics*

• Only 6 to 20 percent of patients are offered trial participation by their physicians. **

• Only 8% of all physicians participate in more than one trial
  • 87% of all physicians are not involved in clinical trials
  • 38% of investigators only conduct one trial


More challenges…

• Many new compounds require high number of patients to show efficacy.

• Complex study design and protocols/ # of assessments.*
  Protocol length increased with 18 pages
  Number of eligibility criteria rose 23 %
  Number of protocol procedures (lab/heart/imaging/questionnaires/…) rose by 48 %
  (especially in oncology/pain)
  Median enterable fields in the CRFs rose by 103 %

• Regulatory requirements

• Pressure and time constrains on academic clinics

• Ever increasing costs

* Joseph, D, Pfizer US, presented at DIA Clinical Forum 2010
And you thought you had seen it all…

HYDERABAD: A pharmaceutical firm's trials fell short when a volunteer tried to escape from their right leg. On March 22, the clinical trials and its executive team changed his mind and offered to send him back to their problems for understanding his leg. After a round of trials, he was offered a new option to escape. However, the volunteer said he had injuries on my right leg.
And now what???

- We need the sites to love us
  - Ease their burden
  - Focus on the important things

- We need to reach the patients
  - Use smart recruitment platforms, e.g. Facebook, TrialBee, or MyClinicalTrialLocator
  - Reach patients at their home or work
  - Electronic patient diaries

- We need improved processes and tools
  - The eCRFs of today are capable!
Fundamental change in project management

Know where you have your problem(s):

• The site
• The country
• The CRF
• The monitor
• The patient
• The …

• As soon as data is in, you have another data point to help you optimize your study

• You need immediate, accurate and clean data!
Immediate and clean data

Data input

• Data Management
• Drug logistics
• Project Management
• Site Management
• Randomisation
• Metric Analysis

Study Management

Informed decisions

Adaptation from Rosenberg, M, President & CEO Health Decisions, presented at DIA Clinical Forum 2010
Risk Based Monitoring

Focus on parameters that would make a critical difference to data quality and patient safety

Different risks:

- Fixed Risks
  - Those related to a trial protocol such as the therapeutic area, drug safety profile, target product profile

- Study Site Risks
  - Site experience, location and the number of study nurses

- Dynamic Risks
  - Real-time evaluation of risk and involve enrollment rate, protocol deviations and adverse events.
Risk Based Monitoring, continued

*Decision points for determining when to visit and what to monitor*

- Data quality
- Patient safety
- How many patients have been recruited
- How much to SDV

- This can actually help the sites actually *manage* the study, not burden them with unnecessary visits
Integrate: Compliance

Immediate response to why the medication was dispensed, follow up in a patient diary and possibly by the study site. If needed, a reminder is sent to the patient and/or the study site.
Integrate: ECG

Immediate read of ECG, follow up by the investigator
As soon as the SAE is filled in the eCRF, a populated SAE report is sent to the pharmacovigilance department, but also all data directly imported into the pharmacovigilance system, reports can be created in “real-time”, no delays and the authorities get the right data immediately – no reconciliation!!
ICH E2B

### Adverse events

<table>
<thead>
<tr>
<th>#</th>
<th>Event</th>
<th>Start date</th>
<th>Stop date</th>
<th>Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>HEAD TRAUMA</td>
<td>2011 Jul 1</td>
<td>-</td>
<td>Severe</td>
</tr>
</tbody>
</table>

**Causality** Not yet assessable  
**Action** None  
**Outcome** Not recovered  
**Serious** Yes

This adverse event should be recorded on a special form (available at [ICH E2B Reports/Documentation link](#)) and forwarded to the Drug Safety Office by fax within 24 hours of learning its occurrence.

### Patient documents

The document(s) highlighted below was generated. Please review and take appropriate actions.

#### Document / Initiated

- [ ] E2B XML  
- [ ] ScrNo 3:01

**Signed** N/A  
**Submit**

---

**ICH ICSR message with E2B elements**

<table>
<thead>
<tr>
<th>Message Type</th>
<th>ich/vari</th>
</tr>
</thead>
<tbody>
<tr>
<td>Message Format Version</td>
<td>2</td>
</tr>
<tr>
<td>Message Format Release</td>
<td>1</td>
</tr>
<tr>
<td>Message Number</td>
<td>VIEDOC_14_3</td>
</tr>
<tr>
<td>Message Sender Identifier</td>
<td>POC</td>
</tr>
<tr>
<td>Message Receiver Identifier</td>
<td>Safety worldwide</td>
</tr>
<tr>
<td>Message Data Format</td>
<td>CCYYMMDD</td>
</tr>
<tr>
<td>Message Date</td>
<td>20110701</td>
</tr>
</tbody>
</table>

**Safety Report**

- **Report Version**: 1  
- **Report Id**: VIEDOC_14_3711  
- **Primary Source Country**: JAPAN  
- **Transmission Date Format**: CCYYMMDD  
- **Transmission Date**: 20110701  
- **Report Type**: Report from study

**Seriousness**

Serious
Payments per completed, monitored visits
Patient registries – presentations in real time

- Graph per patient
- Comparisons between multiple patients
- Per study site
- Comparisons between sites
Clinical Data Interchange Standards Consortium

A Reference for the Rest of Us!
FREE eTips at dummies.com

Dr. Majd Mirza
CDISC & Regulatory Authorities

Recently the FDA gave a clear message that they want data submitted in the CDISC SDTM, ADaM and define.xml formats. If not, they can refuse to accept your NDA. By 2014!

EMA is considering it, for 2014/15

This will affect your trials! You have to be CDISC compliant.
Many functions with different needs want to access the data in different formats.
Inefficiencies in the current (previous) process

3 Weeks of Data Manipulation – 36 pages taped together to explore one question

Demographic data here from DEM dataset

Patient#1234

Past Medical History data here from MEDH dataset

Laboratory data here from LAB dataset

Adverse Event data here from AE dataset

Concomitant Meds data here from Conmed dataset
The standards in CDISC you need to know

Protocol → CRF → Operational database (eCRF)

- Protocol: PRM
- CRF: CDASH
- Operational database (eCRF): ODM

Results → Analysis datasets → Tabulation datasets

- Results: ADaM
- Analysis datasets: SDTM
The Cool Thing!

Harmonization among standards within the clinical research domain and between biomedical/clinical research and healthcare.

CDISC ❤ HL7
What can you do more in an eCRF?

• eTMF – the electronic Trial Master File
• eLearning
• IWRS/Randomisation
• Integration with Lab
• Integration with imaging
• Medical Coding
• Document management
  • Contracts
  • Protocol
  • Ethical Committee(s)
  • Regulatory Authority (ies)
• Adaptive design
Conclusion

• Focus on patient safety, recruitment and retention

• The technical and possibilities are there for your study. And the costs are actually lower than the old process.

• User friendliness!

• Online data and being adaptive to changes essential in recruiting and retaining patients.

• Don’t look at the technology, look at the processes that makes sense and are intuitive to follow – primarily from the study site perspective.
Pharma Consulting Group
Winner of 3 business awards in Sweden for stability and growth –, “DI Gazelle”, “VA Super Company” and “Bona Postulate Award”