Electronic Data Capture - MACRO

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Agenda

• Purpose of Electronic Data Capture (EDC)
• Regulatory Requirements
• EDC-System „MACRO”
• Clinical Trial Support for ELN by WP 3 (CICS)
• Costs
Purpose of Electronic Data Capture

- Obtain trial data in electronic form for subsequent analysis
- Replace paper-based case report forms by electronic ones (e-CRFs)
- Quality assurance:
  - Perform data validation ("edit checks") during data entry
  - Provide assistance for generating and processing queries
Regulatory Requirements

- National law
- Good Clinical Practice (GCP-ICH)
- 21 CFR Part 11 (Electronic Records)
- [EU-GMP Annex 11]
5.5.3 ... the sponsor should:

(a) Ensure and document that the electronic data processing system(s) conforms to the sponsor’s established requirements for **completeness, accuracy, reliability**, and consistent intended performance (i.e., validation).

(b) Maintain **SOPs** for using these systems.

(c) Ensure that the systems are designed to permit data changes in such a way that the **data changes are documented** and that there is no deletion of entered data (i.e., maintain an audit trail, data trail, edit trail).

(d) Maintain a security system that prevents unauthorized access to the data.

...
21 CFR Part 11

• Electronic Records
  - Authenticity
  - Integrity
  - Confidentiality
  - Non-Repudiability

• Electronic Signatures
  - Identification codes & passwords
Requirements for Use in Clinical Trials

- GCP-conformant system
- Vendor using validated software development process
- Validated installation
- Implementation and validation of electronic CRFs
- Registration of authorized users
- User training
• Vendor: InferMed Ltd, London
  - www.infermed.com

• Architecture: Client/Server
  - “Network client”
    • Trial design, data entry, monitoring
    • System and user administration
  - “Web client”
    • Data entry, monitoring
  - “Remote client”
    • Data entry, monitoring
    • Trial design
MACRO Architecture
MACRO Features

- GCP-conformant (e.g., audit trail)
- Support for multicentre trials
- Role-based authorization scheme
- Data validation
- Reporting
  - Data management
  - Monitoring
  - Custom
- Trial design tools
MACRO Minimum Client Requirements

- 450 MHz Pentium II with 128 MB RAM and 500 MB free hard disk space
- Windows 2000 Professional or XP Professional
- Screen resolution of 1024 x 768
- Web client:
  - Internet Explorer (IE) 5.5 or 6.0 with high (128-bit) encryption pack
- Remote client:
  - Local database: MSDE 2000 or SQL Server 2000
• e-CRFs mostly analogous to paper CRFs
  - visits
  - e-forms
• Data types and structures
  - text, date, integer, value + unit
  - repeats
  - special structures for laboratory data
• Programmable plausibility checks
• e-CRF library
Example e-CRF

Subject
HIDIT/mhh/NA259

CoverScreeningLaboratory: Baseline Normal (Beginning of week 2 week 4 week 8 week 12 week 18 week 24 visit: Treatment week 2 27/12/2004 eform: Laboratory

Laboratory values

<table>
<thead>
<tr>
<th>Hematology</th>
<th>Value</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>13.80</td>
<td></td>
</tr>
<tr>
<td>Leucocytes (10^3/µl)</td>
<td>5,10</td>
<td></td>
</tr>
<tr>
<td>Monocytes (10^3/µl)</td>
<td>0,40</td>
<td></td>
</tr>
<tr>
<td>Neutrophils (10^3/µl)</td>
<td>2,80</td>
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</tr>
<tr>
<td>Eosinophils (10^3/µl)</td>
<td>0,10</td>
<td></td>
</tr>
<tr>
<td>Basophils (10^3/µl)</td>
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</tr>
<tr>
<td>Lymphocytes (10^3/µl)</td>
<td>1,80</td>
<td></td>
</tr>
<tr>
<td>Platelets (10^3/µl)</td>
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<tr>
<td>MCV (fl) (optional)</td>
<td>91,30</td>
<td></td>
</tr>
<tr>
<td>Prothrombin time (sec.)</td>
<td>14,20</td>
<td></td>
</tr>
</tbody>
</table>
### Security reports
- Security functions
- Roles
- Users
- User login activity
- Failed login attempts
- User roles
- Password policy

### Data reports
- Data views
- Site recruitment
- Changed data
- eCRF summary
- Subject summary
- Data
- Missing data by site
- Missing data by subject
- Missing data by form
- Missing data
- Out of range lab data
- Discrepancy Count
- Done SDVs / changed data

### Metadata reports
- Sites
- Study sites
- Units of measurement
- CTC Schemes
- Laboratory normal ranges
- Laboratories
- Laboratory sites
- Clinical test groups
- Clinical tests
- CDISC
- Standard data formats
- Study phases
- Validation types
- Trial types
- Countries
- Reserved words
- Studies

**Options**
- Display / print
- Excel
- CSV
• Operational since April 2006
• Network security (firewall)
• Implemented trials: 3
Trial Implementation by WP 3

• WP 3 can provide:
  - CRF design consulting (in collaboration with WP 17), including specification of data dictionary
  - e-CRF implementation
  - e-CRF validation
  - User management
  - User training
  - Help desk

• WP 3 cannot provide:
  - data entry from paper forms on any relevant scale
## Trial Implementation Procedure

<table>
<thead>
<tr>
<th>Step</th>
<th>WP3/Sponsor</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Trial protocol finalized</td>
<td>Sponsor</td>
</tr>
<tr>
<td>• Specification of Data Dictionary</td>
<td>both</td>
</tr>
<tr>
<td>• Implementation of e-CRFs</td>
<td>WP3</td>
</tr>
<tr>
<td>• Review of e-CRFs</td>
<td>Sponsor</td>
</tr>
<tr>
<td>• Validation of e-CRFs</td>
<td>WP3</td>
</tr>
<tr>
<td>• Site and user registration</td>
<td>both</td>
</tr>
<tr>
<td>• User training (if necessary)</td>
<td>WP3</td>
</tr>
<tr>
<td>• Activation of trial data entry</td>
<td>WP3</td>
</tr>
</tbody>
</table>
Minimum Data Dictionary Content

• Patient identification
• For each visit:
  - Scheduled time (range)
  - Items (variables) to be documented
• For each item:
  - Data type (text, number, date, choice, selection...)
  - Coding used
  - For laboratory tests:
    • Range of possible values
    • Range of likely (not frequent !) values
Costs

• Additional costs to be bourne by the trial sponsor will arise from:
  - Named users: 600 € per user + 100 € per user and year
  - Training of system users
  - Trials related to drug registration or other commercial purposes (substantial amounts !)

• Additional costs may arise for implementation, validation and management of either numerous trials or extremely complex trials
Summary

• WP 3 operates a validated installation of the GCP-conformant data capture software MACRO
• The system is available for clinical trials conducted by the ELN
• WP 3 provides e-CRF design and validation
• Additional costs may arise, e.g. for user licenses
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