Central Monitoring by Data Management

Edit checks, logical checks, automatic review of data, trend analyses…

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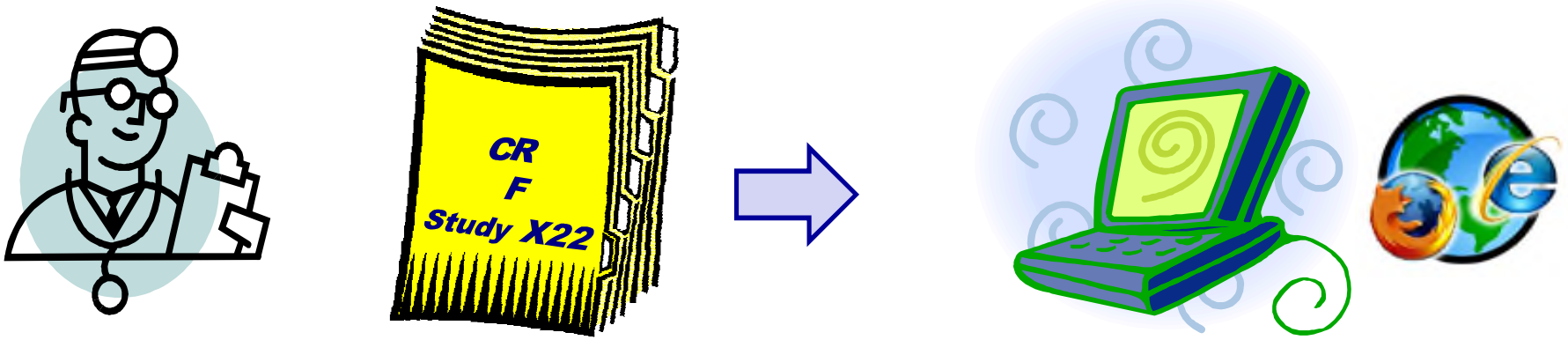
Agenda

- DM Contribution to Data Quality
  - Data Management Plan
  - Edit checks
  - External Data
  - Listings and Reports
- RBQM & RBM
- Central Monitoring

CRF: from Paper to EDC



- **New Workflow => New Tempo**

Near Real Time Data Flow

Sites

CRF

DM

Reviewers

Lab Data

EDC/CDM

Dashboard

Study team

Patients

eCOA

CRA

Data Management Plan

- Team approach to develop the DMP with all stakeholders
- Identify and define the personnel and roles involved with decision making, data collection, data handling and data quality control

Edit Checks (1/2)

- On-line Edit Checks
  - Triggered immediatly after an entry (within the screen/page)
    - Range of acceptable values (threshold, limit…)
    - Data type (numeric, text…)
    - Derived or calculated value
    - Date

Is there a limit?

Edit Checks (2/2)

- Off-line Edit Checks
  - Triggered « nightly » at the server level (CDMS)
    - Cross-domain to ensure consistency between different sections of the CRF

Edit checks must be appropriate

External Data : ePRO, Lab Data…

- Which external data in the eCRF/EDC?
  - to streamline the process
  - for the patient benefit
- Which actors should be allowed to view external data?
  - Unblinding risks
- When in the study time line?
  - At the patient pre-selection time
  - Study on going

External Data: Review Committees

- Academic Research Organisation, Central Reader, Data Monitoring Committee
  - How to collect the assessments or analyses?
    - External documents with signatures
    - In a « mixed » system (hospital)
      - « validated » with an audit-trail (or not) => due diligence
    - In the eCRF (ID/password for the experts)
  - When in the study time line?
    - At the patient pre-selection time
    - Study on going

Reports and listings

- Reports and listings for
  - Study team
  - Data reviews
  - Risk Based Monitoring
  - QA
- Standard listings (dump)
- Pre-configured business intelligence tools

Reports and listings

- Ad-hoc reports
  - Complex logics (protocol compliance)
  - Data analytics with statistical functions
    - Trend Analyses and **Outliers**
  - Draft Clinical Study report
- Validation of edit checks and reports
  - Reviewer
    - Clinical, Statistical, Programming expertise
  - Test datasets

Reports and listings

- Expected Actions by the Reviewer
  - Queries to investigate the discrepancies
  - Site re-training
  - Non-compliance with protocol
    - Eventually report to ethics
  - Suspicion of data fraud

    =>RBM and RBQM

RBQM & RBM

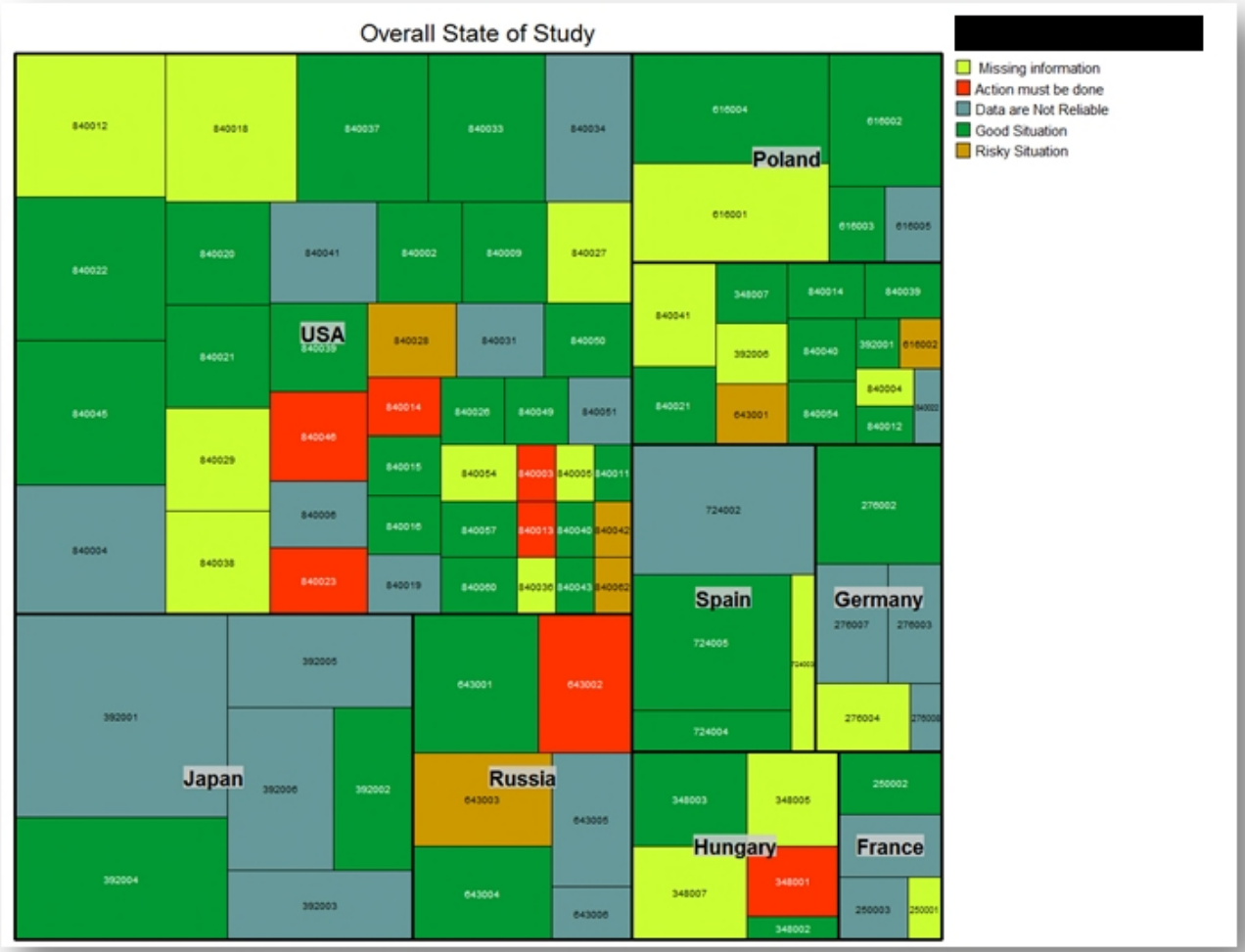
- Impact on Data Quality and Data Integrity?
- Challenges for Clinical Data Managers
- Interactions with other stakeholders
  - Clinical Operations
  - Investigators
- New Role and new Skill for DMs?

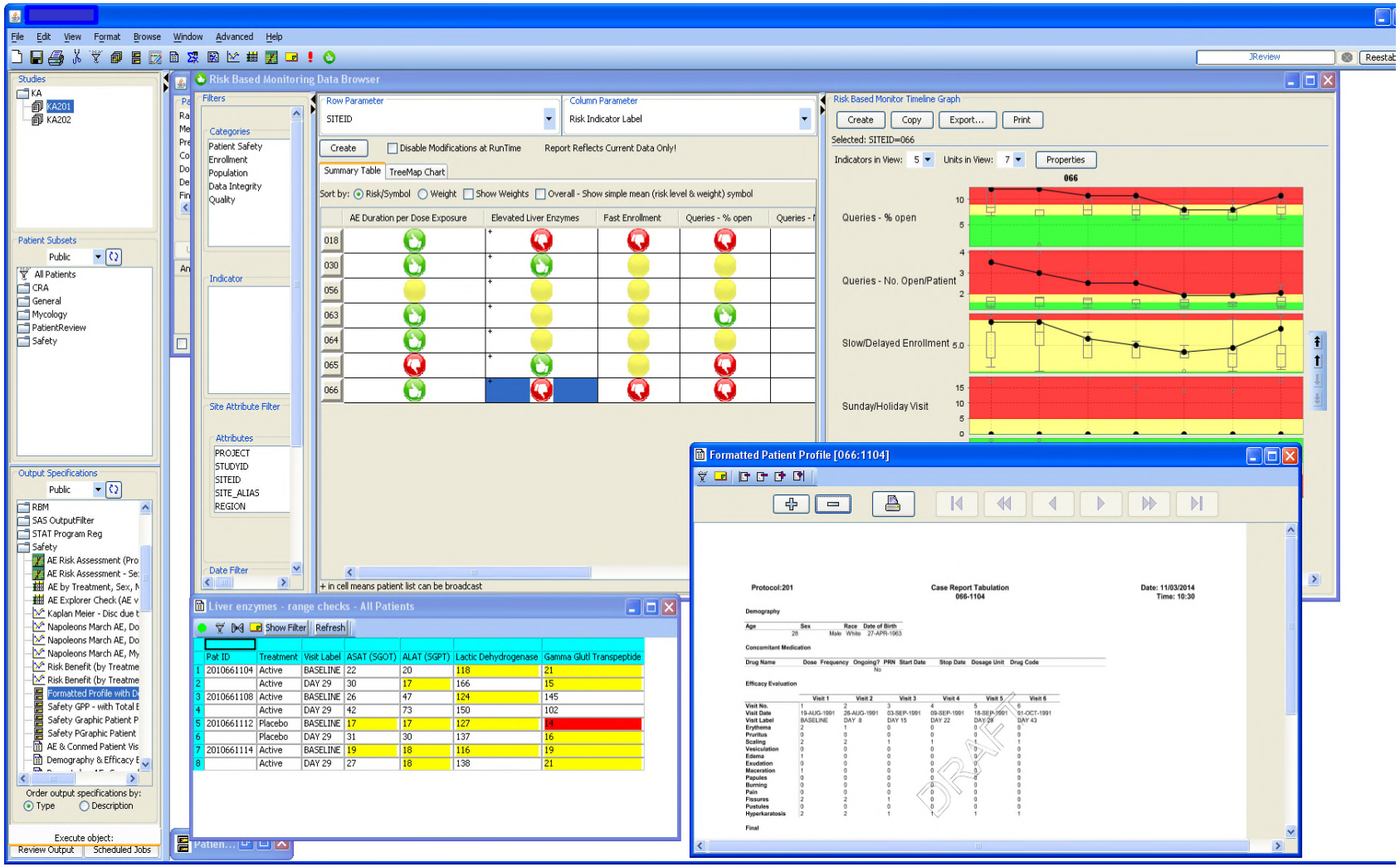
Quality by Design eCRF

- Some key success factors:
  - A stabilized Protocol
  - A team Approach
  - A Risk Analysis
  - A Data Collection Strategy
  - A realistic Timeline

Central Monitoring

Dashboard


Overall State of Study
Missing information
Action must be done
Data are Not Reliable
Good Situation
Risky Situation
Poland
USA
Japan
Russia
Spain
Germany
Hungary
France


File Edit View Format Browse Window Advanced Help
Studies
KA
KA201
KA202
Patient Subsets
Public
All Patients
CRA
General
Mycology
PatientReview
Safety
Output Specifications
Public
RBM
SAS OutputFilter
STAT Program Reg
Safety
Order output specifications by:
Type
Description
Execute object:
Review Output
Scheduled Jobs
Risk Based Monitoring Data Browser
Filters
Categories
Patient Safety
Enrollment
Population
Data Integrity
Quality
Indicator
Site Attribute Filter
Attributes
PROJECT
STUDYID
SITEID
SITE_ALIAS
REGION
Date Filter
Row Parameter
SITEID
Column Parameter
Risk Indicator Label
Create
Disable Modifications at RunTime
Report Reflects Current Data Only!
Summary Table
TreeMap Chart
Sort by: Risk/Symbol Weight Show Weights Overall - Show simple mean (risk level & weight) symbol
AE Duration per Dose Exposure
Elevated Liver Enzymes
Fast Enrollment
Queries - % open
018
030
056
063
064
065
066
+ in cell means patient list can be broadcast
Risk Based Monitor Timeline Graph
Create
Copy
Export...
Print
Selected: SITEID=066
Indicators in View: 5
Units in View: 7
Properties
066
Queries - % open
Queries - No. Open/Patient
Slow/Delayed Enrollment
Sunday/Holiday Visit
Liver enzymes - range checks - All Patients
Show Filter
Refresh
Pat ID
Treatment
Visit Label
ASAT (SGOT)
ALAT (SGPT)
Lactic Dehydrogenase
Gamma Glutl Transpeptide
1 2010661104 Active BASELINE 22 20 118 21
2 Active DAY 29 30 17 166 15
3 2010661108 Active BASELINE 26 47 124 145
4 Active DAY 29 42 73 150 102
5 2010661112 Placebo BASELINE 17 17 127 14
6 Placebo DAY 29 31 30 137 16
7 2010661114 Active BASELINE 19 18 116 19
8 Active DAY 29 27 18 138 21
Formatted Patient Profile [066:1104]
Protocol:201
Case Report Tabulation
066-1104
Date: 11/03/2014
Time: 10:30
Demography
Concomitant Medication
Efficacy Evaluation
DRAFT

RISKS FACTORS

Deviation	•Low Screen Failure rate •Low Dropout Rate •Low AE Reporting	
Inspection Weighting	•Trial Priority •High Enroller	
Issues at Site	•Re-Enrolled Patients •Non-I/E Protocol Deviation •Multiple Trials with the Sponsor • # I/E Protocol Deviation	• High Screen Failure Rate • High Enrollment Rate • High Dropout Rate
Monitoring	•Low frequency of monitoring visits •Late Monitoring after FPFV •High site un-monitored duration •High CRA Workload	
Project delays	•High SAE Reporting •Country	
Site Incident	•Low SAE Reporting •Low Medical History Reporting •Low Concomitant Medication Reporting •High Site Start Time	• High Queries per CRF • Low Queries per CFR • High Querie Time • Late Entry of CRF Data
Monitoring Report Issues	•Drug Accountability issue •Informed consent issue •Issues not closed	• High monitoring issues • Low monitoring issues

KRIs

Other Risks

- Role segmentation and Outsourcing
  - Sponsor
  - Investigators
  - CROs
  - Service Providers
  - Data Analyst, IT/IS, Biostatistician, DM
- Qualification and Training
- Time

Summary

- Change Management
  - Coordination between actors
  - New skills
  - New job descriptions
  - New tools
  - Proactive/Adaptive instead of reactive Monitoring
- Process integration
  - Added Quality
  - More efficient use of ressources

Thank you for your attention