
Medical Data Review in Exploratory Drug Development

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Phuse 2009 AD06

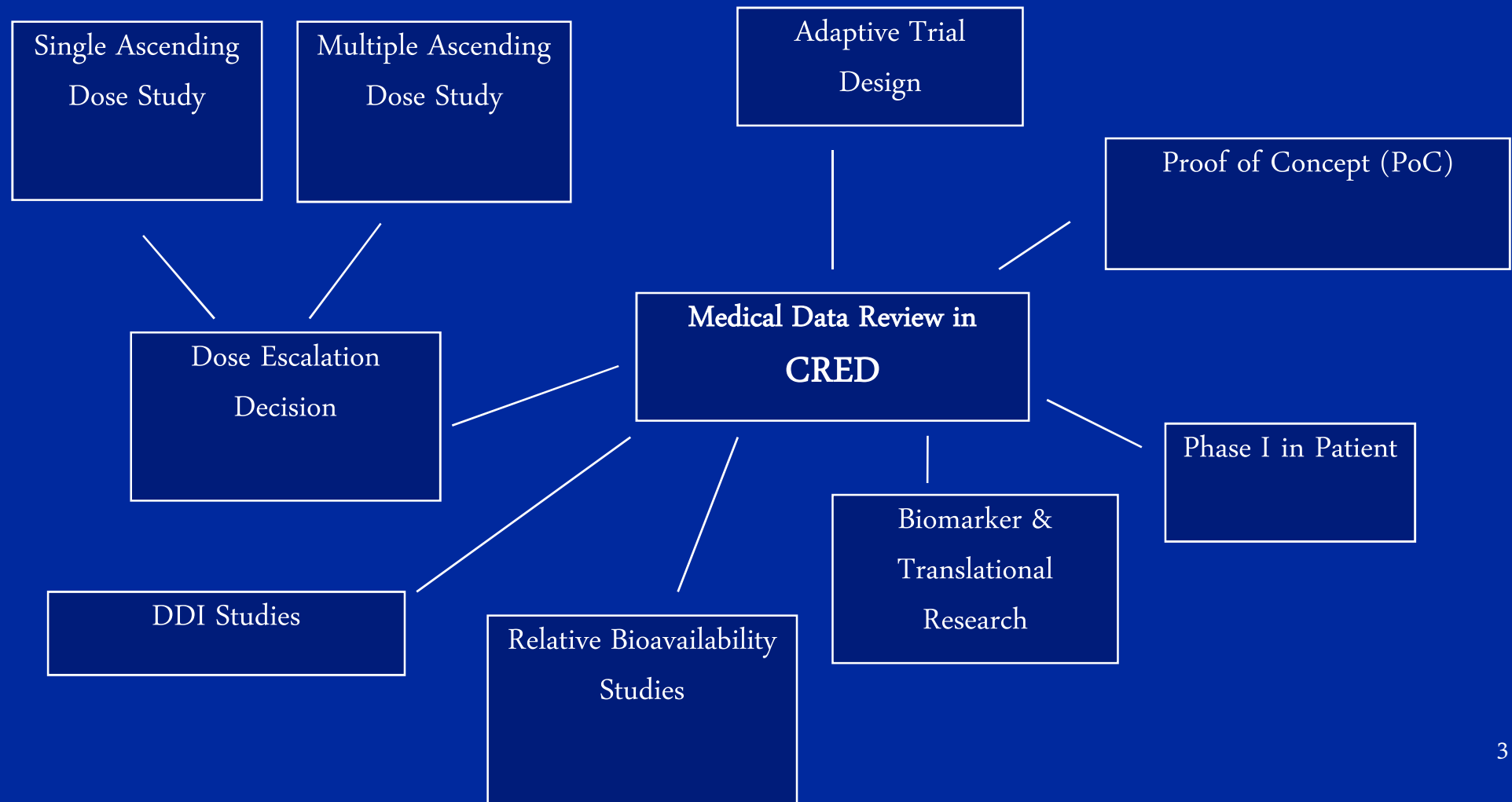
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Topics

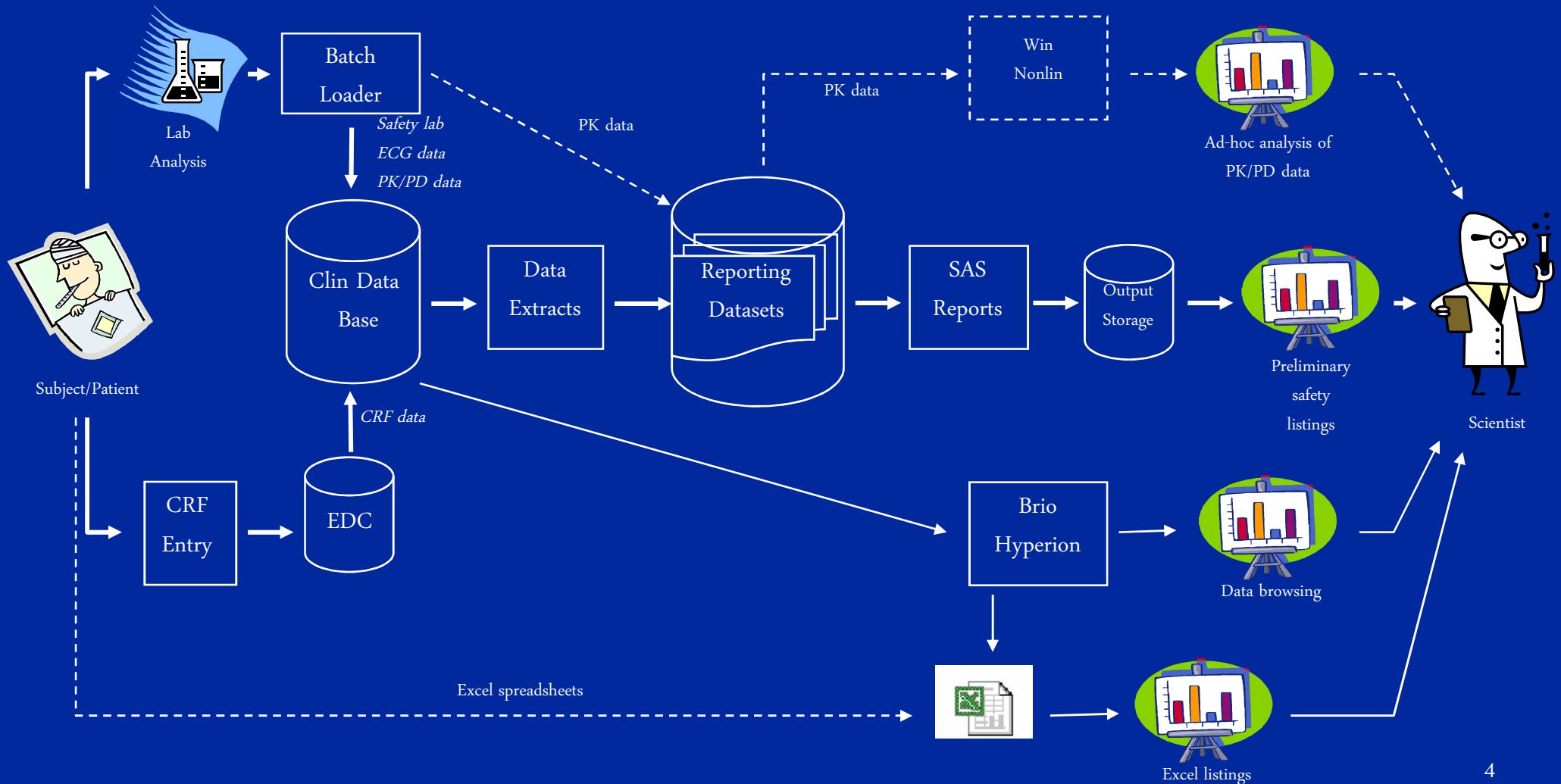


- Current medical data review during study conduct
- Medical requirements
- Planned medical data review
- Templates for medical data review
- What is Tibco Spotfire
- Spotfire Demonstration
- Spotfire Whish List
- If time permits: Informatics implementation plans

Medical Data Review in “Clinical Research and Exploratory Development” (CRED)



Current Data Flow for Medical Data Review



CRTN/Pt. No.	Age Sex yr	Weight kg	Height cm	Race	Trial Treatment	Treatment Start-End
99801/0004	66 F	65	157	CAUCASIAN	PLACEBO	29OCT1997-21NOV1997
99801/0013	49 F	55	165	ORIENTAL	RO 99-9999 5 g bid	30JUL1997-13OCT1997
99801/0021	53 F	81	157	HISPANIC	RO 99-9999 1 g bid	29JUL1997-19JAN1998
99801/0036	60 F	57	160	CAUCASIAN	RO 99-9999 1 g bid	03NOV1997-13FEB1998

Body System/ Adverse Event	PLACEBO N = 66 No. (%)	RO 99-9999 1g bid N = 81 No. (%)
ALL CAUSES	219	301
Death at Least one AE	56 (85)	73 (90)
Number of AEs		
ALL CAUSES		
Death at Least one AE	39 (59)	36 (44)
Number of AEs	13 (20)	12 (15)
ALL CAUSES NOS	8 (12)	6 (7)
UPPER	3 (5)	7 (9)
STOMACH	2 (3)	8 (10)
INFLAMMATION	6 (9)	4 (5)
ALL CAUSES NOS	6 (9)	2 (2)
UPPER NOS	1 (2)	6 (7)
INFLAMMATION	2 (3)	2 (2)
ALL CAUSES NOS	1 (2)	3 (4)
UPPER NOS	-	2 (2)
INFLAMMATION NOS	2 (3)	-
UPPER NOS	1 (2)	1 (1)
INFLAMMATION NOS	1 (2)	1 (1)

Mean ($\pm$ S.E.M.) Change from Visit-specific Baseline for DIASTOLIC BP (mm HG) over Time

Legend:

- Treatm A 10 MG Period 1 / N=10
- Treatm A 10 MG Period 2 / N=14
- △ Treatm B 50 mg Period 1 / N=14
- ▲ Treatm B 50 mg Period 2 / N=10

Time	Treatm A 10 MG Period 1 / N=10	Treatm A 10 MG Period 2 / N=14	Treatm B 50 mg Period 1 / N=14	Treatm B 50 mg Period 2 / N=10
Pre-Dose	0	0	0	0
30min	-3.5	0.5	0.5	0.5
2h	-1.5	3.2	3.5	4.2
24h	-2.0	2.5	3.5	4.0
48h	-1.8	-1.5	-1.5	-1.5

Current Medical Data Review

- Official source: data listings, summary information, graphs set up in SAS provided by statistics department
- Different data sources are used:
 - Extracts from the clinical data base
 - Processed data
 - Data sets as used for study reporting
- Different software solutions are used: Hyperion, Excel, WinNonlin, SAS, Splus/R
- Based on hard copies and piles of paper
- Calculations are done (sometimes) on the fly

Medical Requirements



- List individual subject data as well as **aggregated** data
- Restrict to **subgroups** of interest
- Display **graphically** actual values and change from baseline for repeated measurements
- Use graphs for reporting of **Adverse Events**
- **Share results** with colleagues
- Allow for **interactivity**, **links** between data...

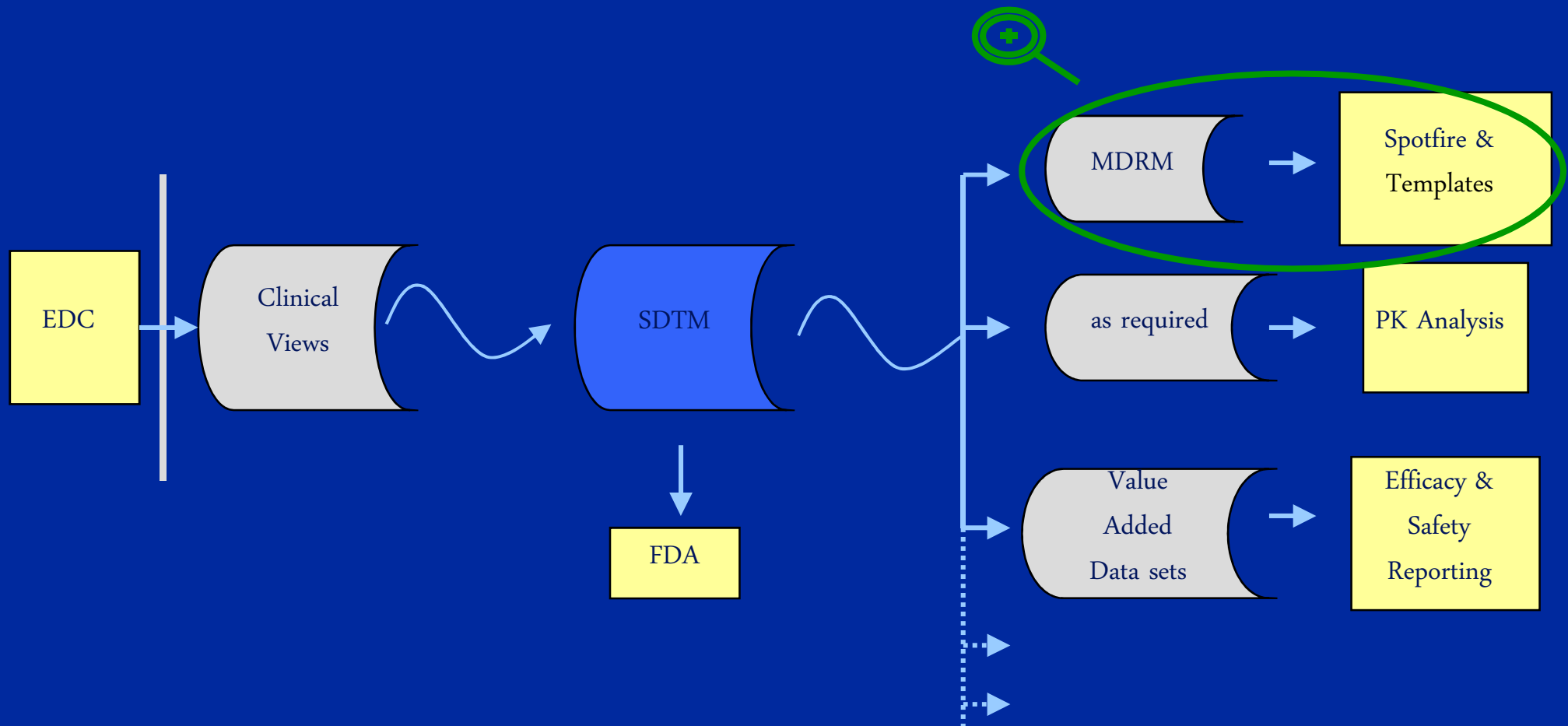
Software Solution and Process Improvement

Based on an assessment of the current environment, a team was formed to look into

- a software solution to allow medical data review according to science requirements
- enhance the data flow and processes to support software solution

→ selection of Tibco Spotfire as software solution and proposal for tailored process and data flow

Planned Data Flow in “Clinical Research and Exploratory Development”



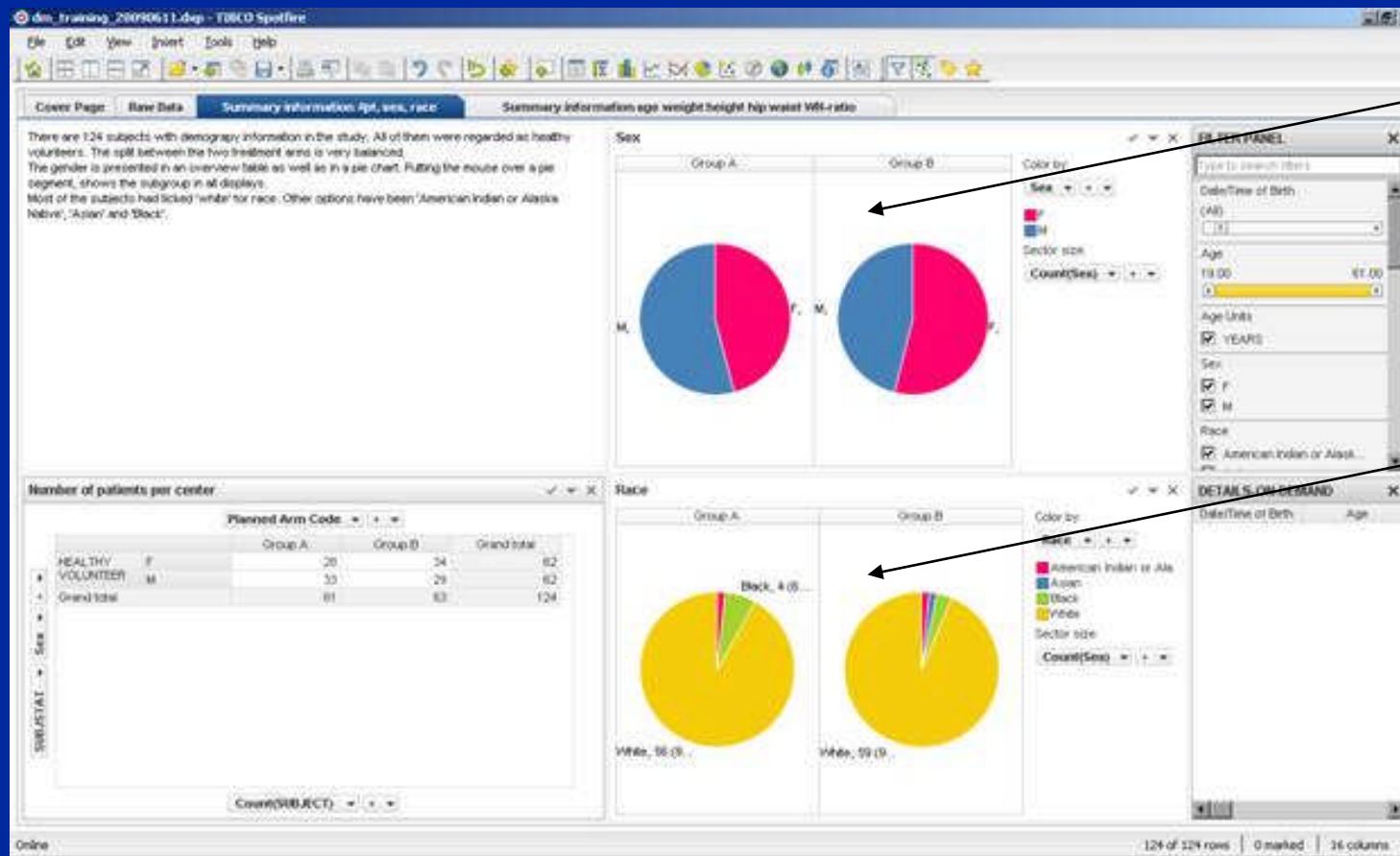
- Stable data model resulting in data sets tailored for medical data review
- Underlying principle: most of the derivations required for medical data review should be programmed up-front; examples for derivations:
 - Study day
 - Baseline calculations
 - Change from baseline
 - Flagging of lab values out of normal range
- Initial domains covered for MDRM: demography (DM), adverse events (AE), lab (LB), ECG (EG), vital signs (VS)

- The Tibco Spotfire is a real time analytical software, allowing the user to mine through large amounts of data quickly and efficiently
- The data can be presented in different visual formats
- Data can be directly opened from a variety of file formats such as SAS, .xls, .txt and .csv files
- The filter device is based on the column content and the number of unique values within each column
- The tool is especially useful, when presenting results to teams

Advantage of the Template Approach

- Do not start with an empty page
- Guided navigation for new Spotfire users
- Copy from study to study ('cookie-cutter' approach)
- Common denominator in terms of data evaluation across study designs
- Results in line with clinical study report
- 'Controlled' environment

TIBCO Spotfire Examples: Viewing of Entire Datasets



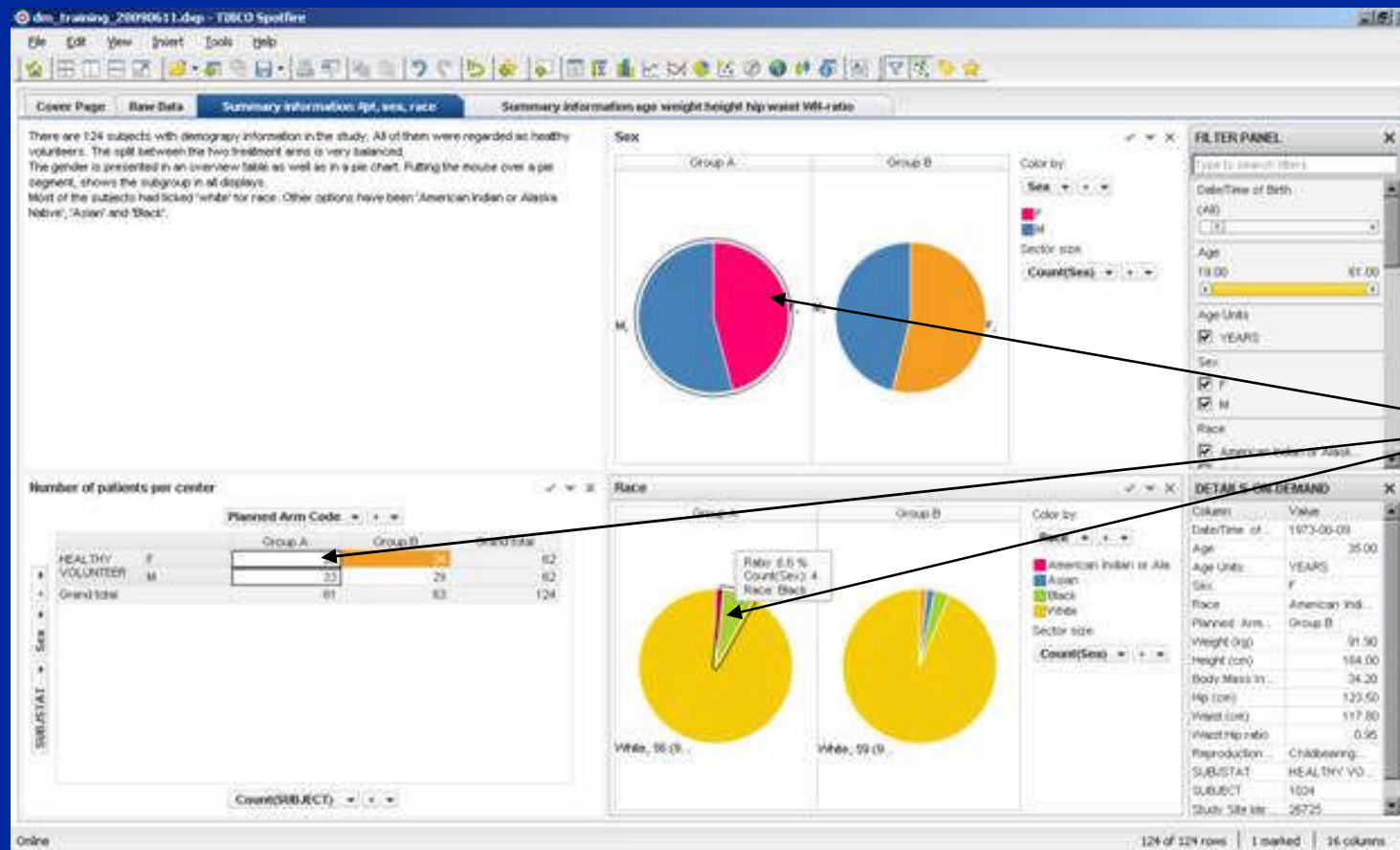
Gender Distribution

Race Distribution

- Sample screen shot of the demographic data template, summarizing gender and race distribution along with the number of subjects enrolled in the study

TIBCO Spotfire Examples: Viewing of Entire Datasets

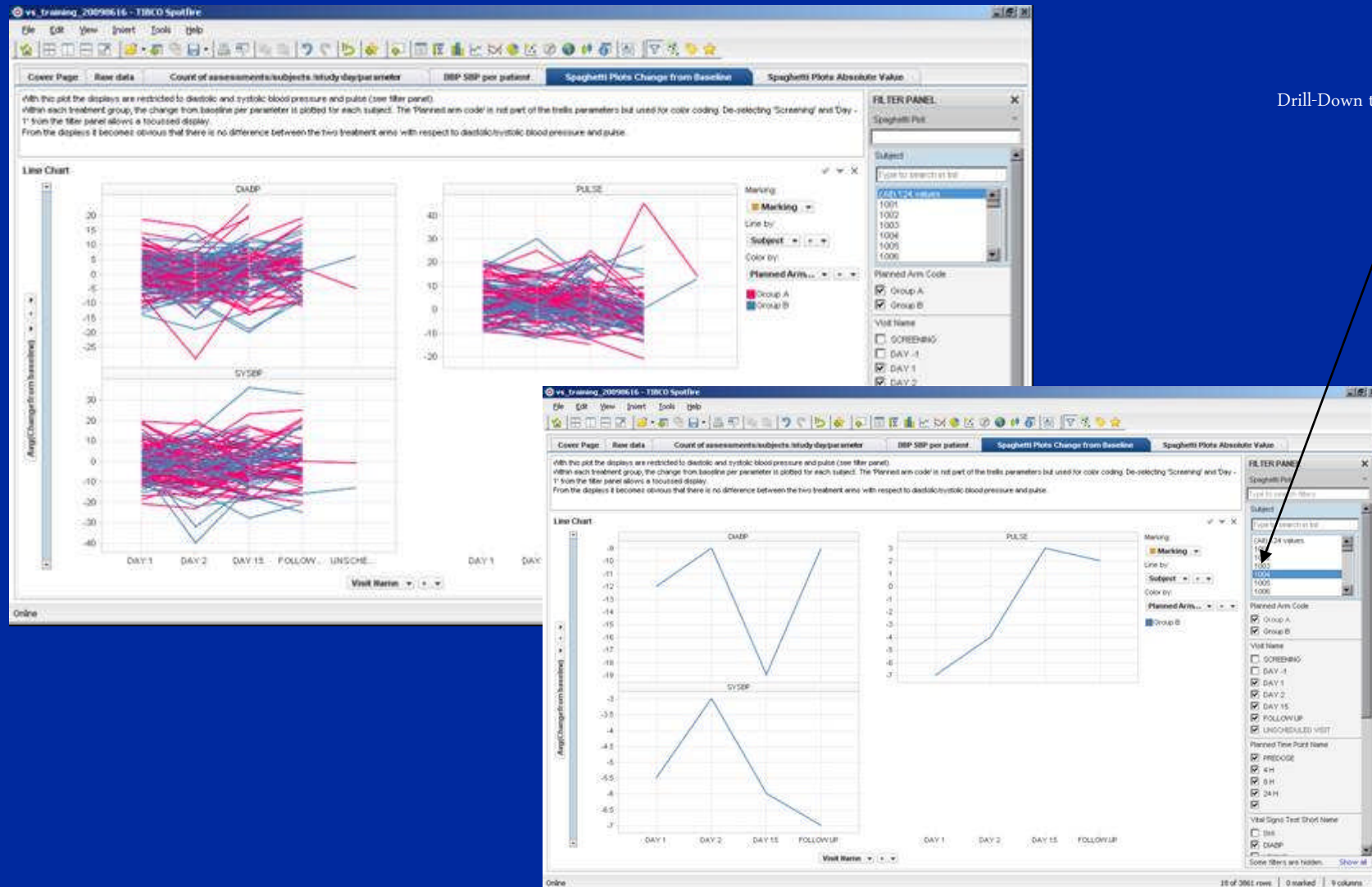
- The templates are interactive and by selecting particular components of one of the pie charts, all other visualizations on the page are updated in real time.



Real time update of data

TIBCO Spotfire Examples: Drill-Down to Subject Level

- One additional aspect is the ability to review large data sets and to drill down to subject level data.

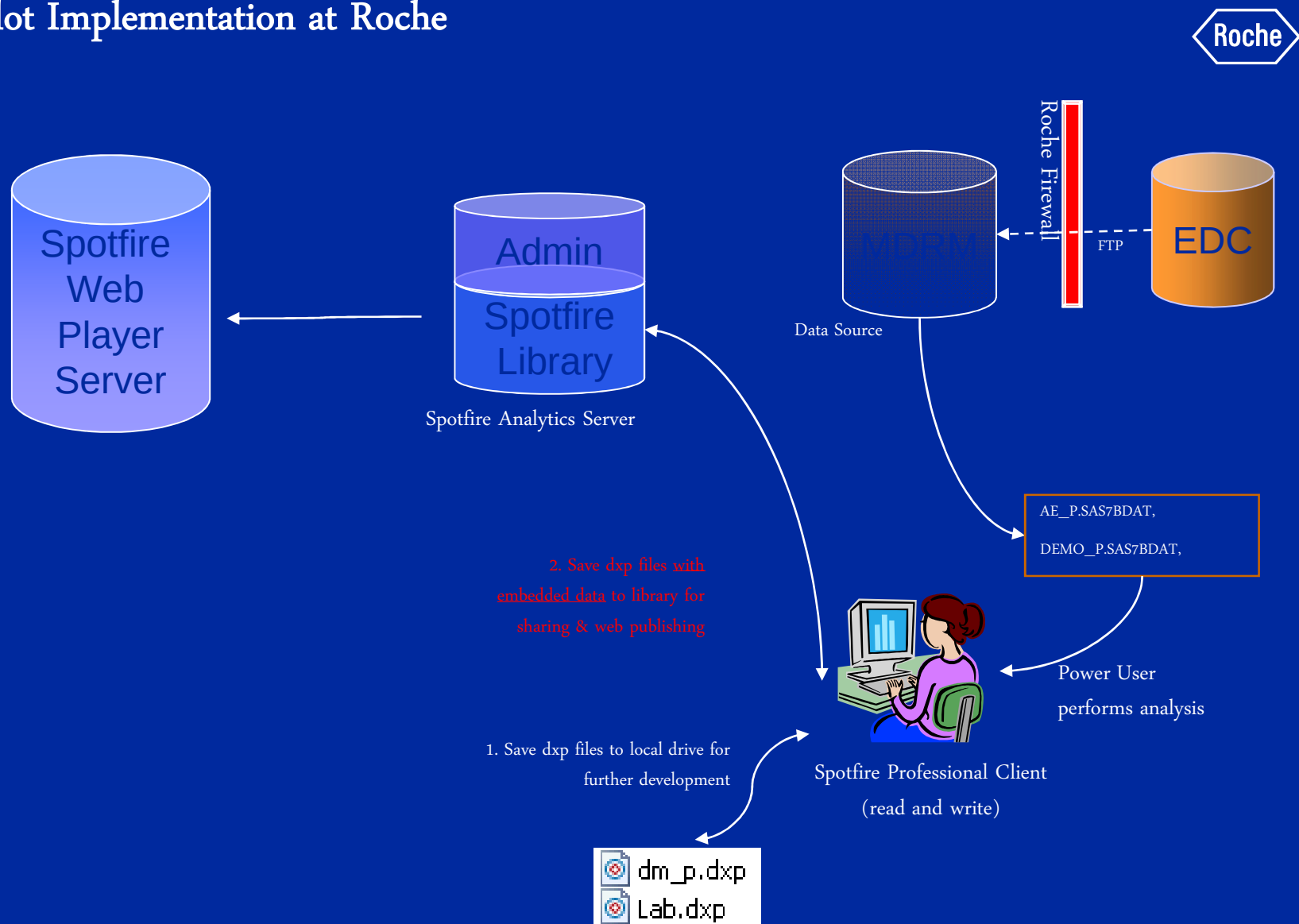


Spotfire Whish List

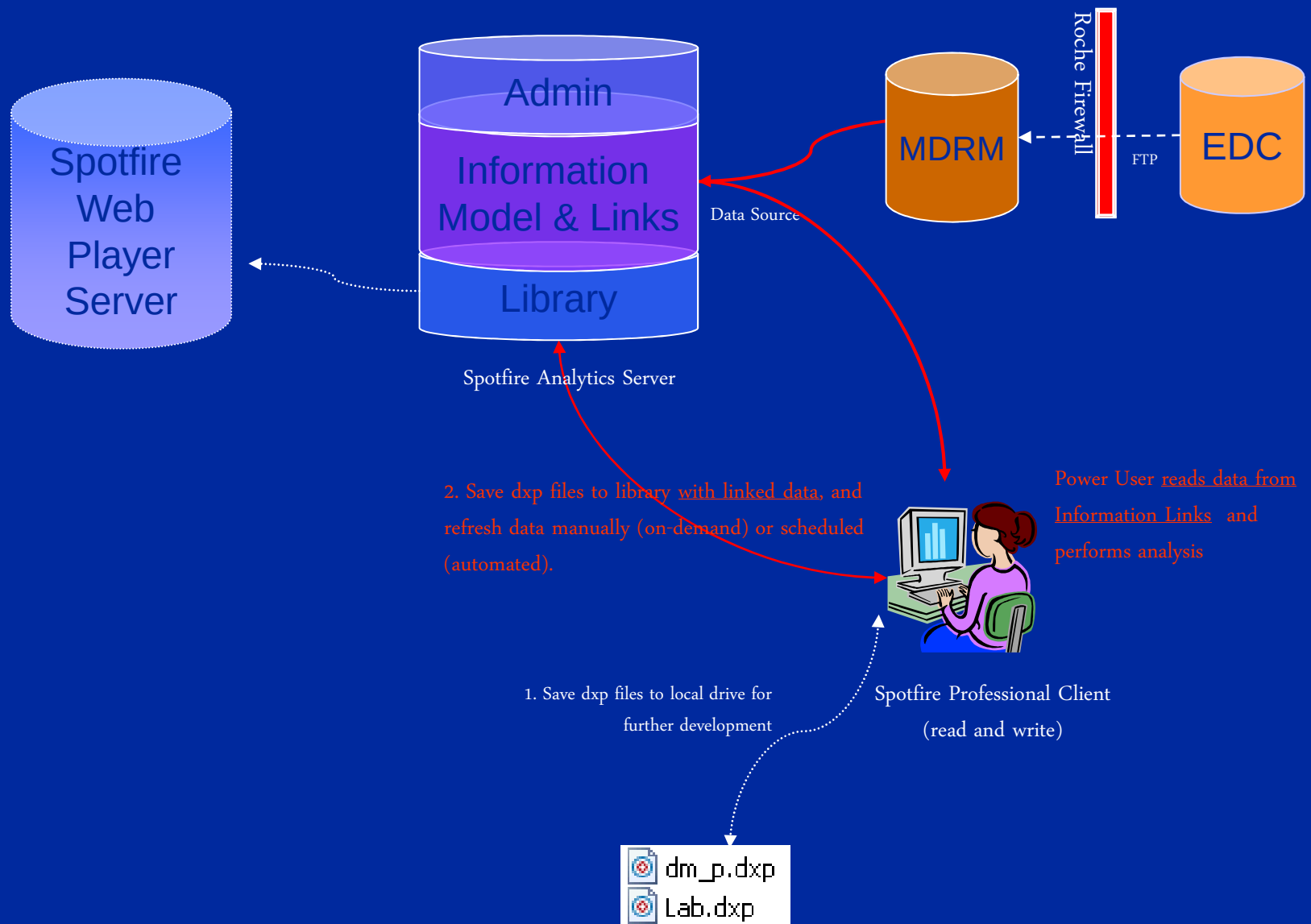


- Audit trail
- Documentation of exploration
- Produce S+ or SAS script to allow reproduction in validated invironment
- Add key graph-types like Kaplan-Meier graphs and error bars

Current Pilot Implementation at Roche



Planned Implementation at Roche



Acknowledgement



Team Members:

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Thank you very much !!!