

Medical Data Review Exploratory Drug Development

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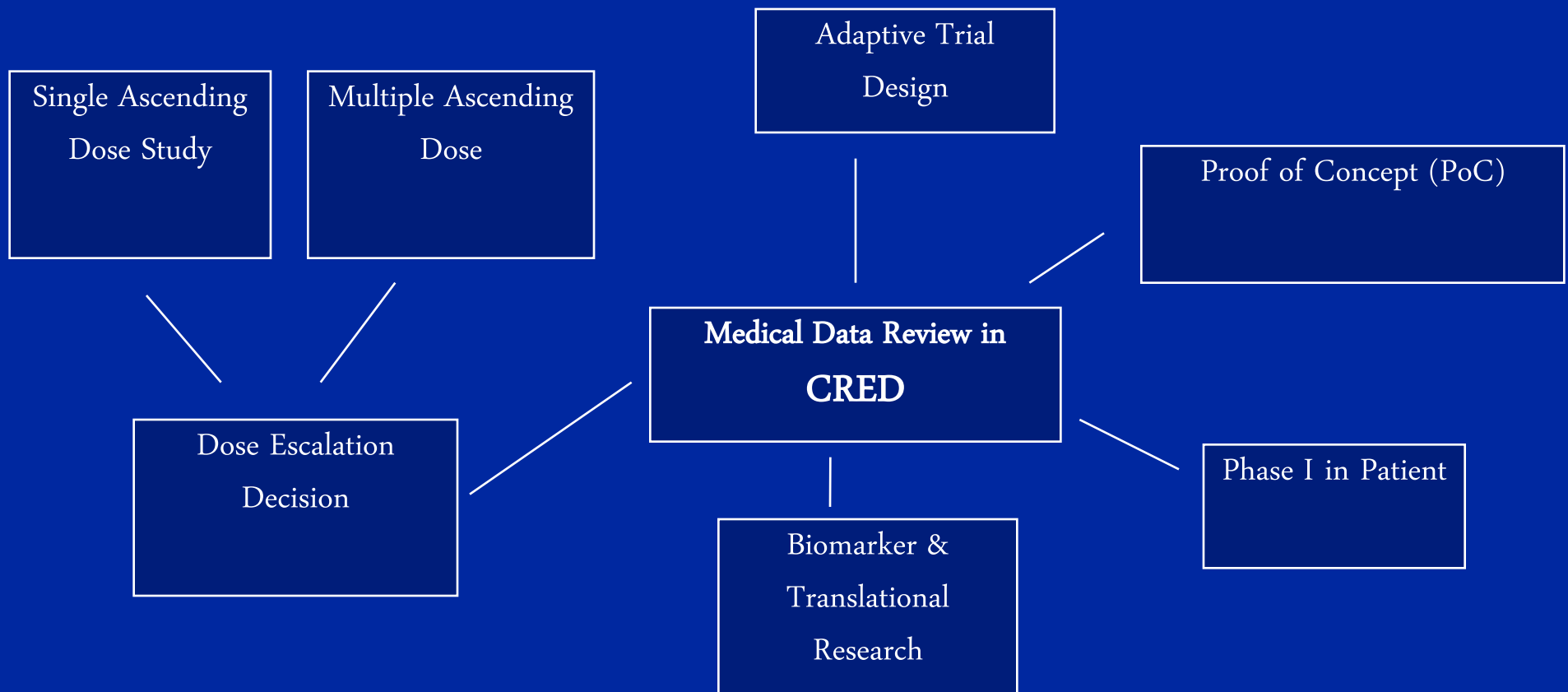
Michaela Jahn and Joshua Haznedar

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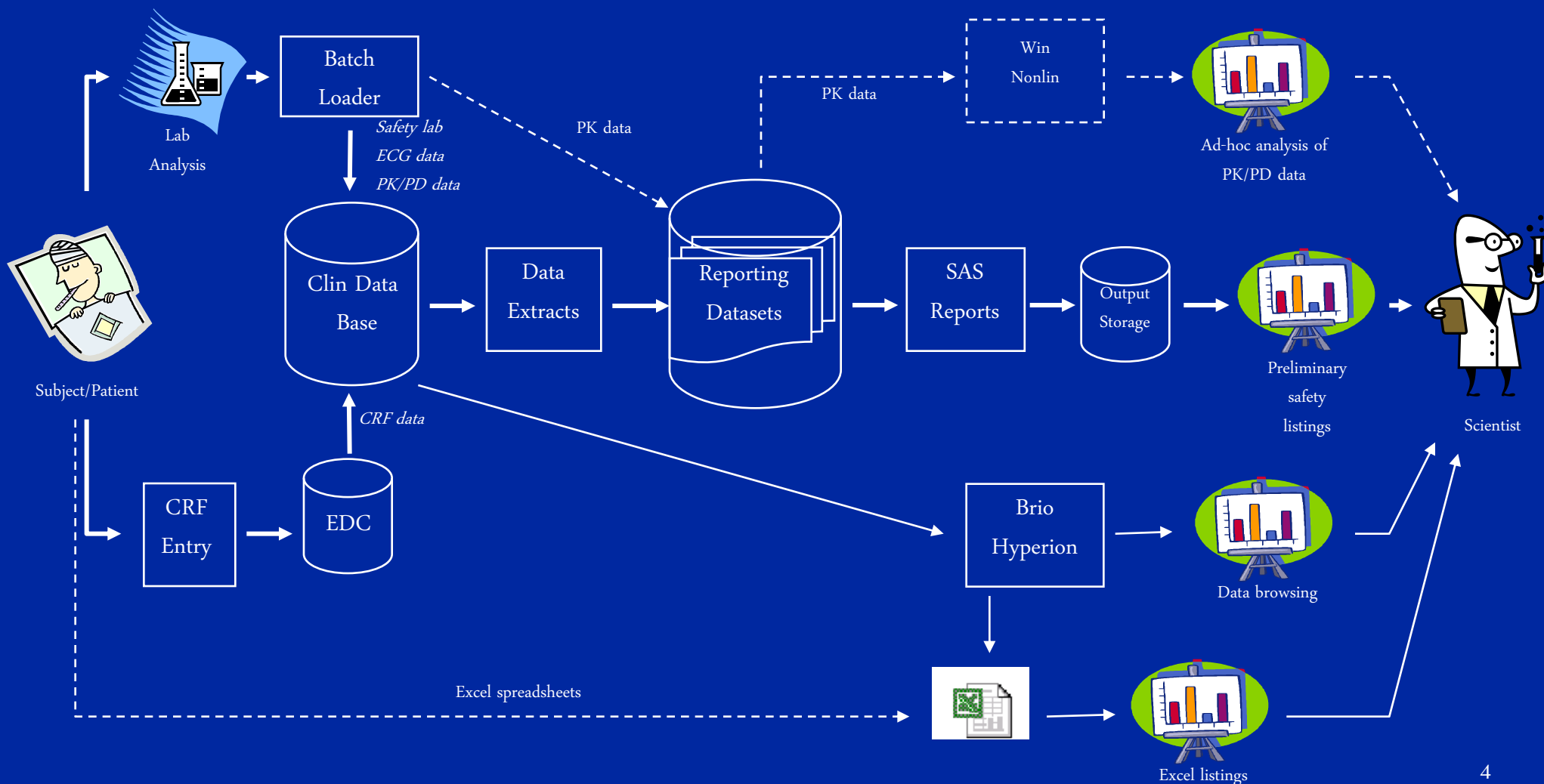
October 20th, 2009

- Relevance of medical data review during study conduct
- Current medical data review during study conduct
- Science requirements
- Planned medical data review
- Templates
- What is Tibco Spotfire
- Spotfire DEMO
- Informatics implementation plans

Study Types in Roche “Clinical Research and Exploratory Development” (CRED)



Current Data Flow for Medical Data Review



Some Examples

Listing of Patient Demographic Data by CRTN/Patient Number

Protocol(s): SAMP-PAR

Analysis: ALL PATIENTS Center: ALL CENTERS

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

Listing of Patients with Adverse Events by Trial Treatment and CRTN/Patient Number

All Adverse Events

Protocol(s): SAMP-PAR

Analysis: ALL PATIENTS Center: ALL CENTERS

Treatment: PLACEBO; N = 66

CRTN/Pt. No. Adverse Event	Age Sex yr	Weight kg	Race	Intensity	Day of Onset	Duration in days	Relation to Trial Treatment	Outcome
99801/0085 CELLULITIS Comment: C/O SWELLING TO L LEG & ANKLE REDNESS NOTED HALF WAY UP LEG TO KNEE. WARM TO TOUCH. TODAY PRESCRIPTION GIVEN.	59 F		CAUCASIAN	MILD	7	17	UNRELATED	RECOVERED
BRONCHITIS NOS				MODERATE	51	58	UNRELATED	RECOVERED
RHEUMATOID ARTHRITIS AGGRAVATED				MODERATE	51	?	UNRELATED	UNRECOVERED
OVERDOSE NOS				MILD	55	4	UNRELATED	RECOVERED
RHINITIS ALLERGIC NOS				MODERATE	67	42	UNRELATED	RECOVERED
BRONCHITIS NOS				MODERATE	143	22	UNRELATED	RECOVERED

Summary of Adverse Events by Body System and Trial Treatment

All Adverse Events

Protocol(s): SAMP-PAR

Analysis: ALL PATIENTS Center: ALL CENTERS

Body System/ Adverse Event	PLACEBO N = 66 No. (%)	RO 99-9999 1g bid N = 81 No. (%)
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ALL BODY SYSTEMS

Total Pts with at Least one AE	56 (85)	73 (90)
Total Number of AEs	219	301

GASTROINTESTINAL DISORDERS

Total Pts With at Least one AE	39 (59)	36 (44)
NAUSEA	13 (20)	12 (15)
DIARRHOEA NOS	8 (12)	6 (7)
ABDOMINAL PAIN UPPER	3 (5)	7 (9)
VOMITING NOS	2 (3)	8 (10)
CONSTIPATION	6 (9)	4 (5)
DYSPEPSIA	6 (9)	2 (2)
ABDOMINAL PAIN NOS	1 (2)	6 (7)
MOUTH ULCERATION	2 (3)	2 (2)
DRY MOUTH	1 (2)	3 (4)
GASTROENTERITIS NOS	-	2 (2)
NAUSEA AND VOMITING	2 (3)	-
FLATULENCE	1 (2)	1 (1)
LOOSE STOOLS	1 (2)	1 (1)

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

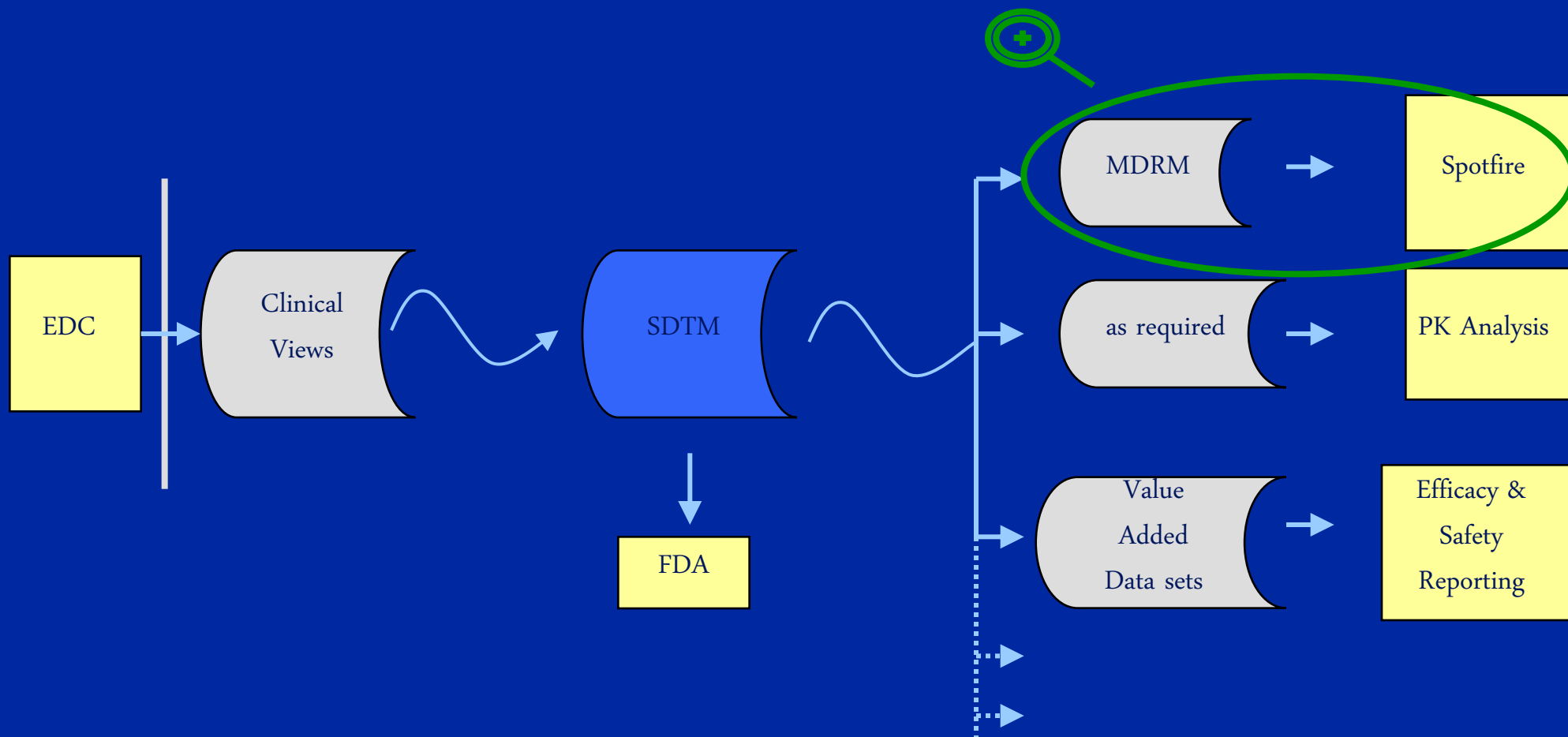
Why an other tool?

- Perform all evaluations on subset of subjects/groups
- List individual subject data as well as aggregated data
- Graphical display of actual values and change from baseline
- Graphical display of the AEs
- Display groups of lab parameters on the same page
- Provide templates
- Share results with colleagues
- Interactivity, links between data...

Benefit of Medical Data Review using Spotfire

- Perform ongoing medical data review
- Evaluate the trial status
- Check on inclusion or exclusion criteria
- Identification of drop-outs / sites
- Evaluate the consistency of data within subject and across subjects
- Reduce data quality issues
- Prepare of interim analyses and management of trial adaptations
- Fast identification and resolution of data quality issues
- Review clinical data faster
- Drill-down from population to subject level
- Identify subgroups of special interest

Planned Data Flow in “Clinical Research and Exploratory Development”



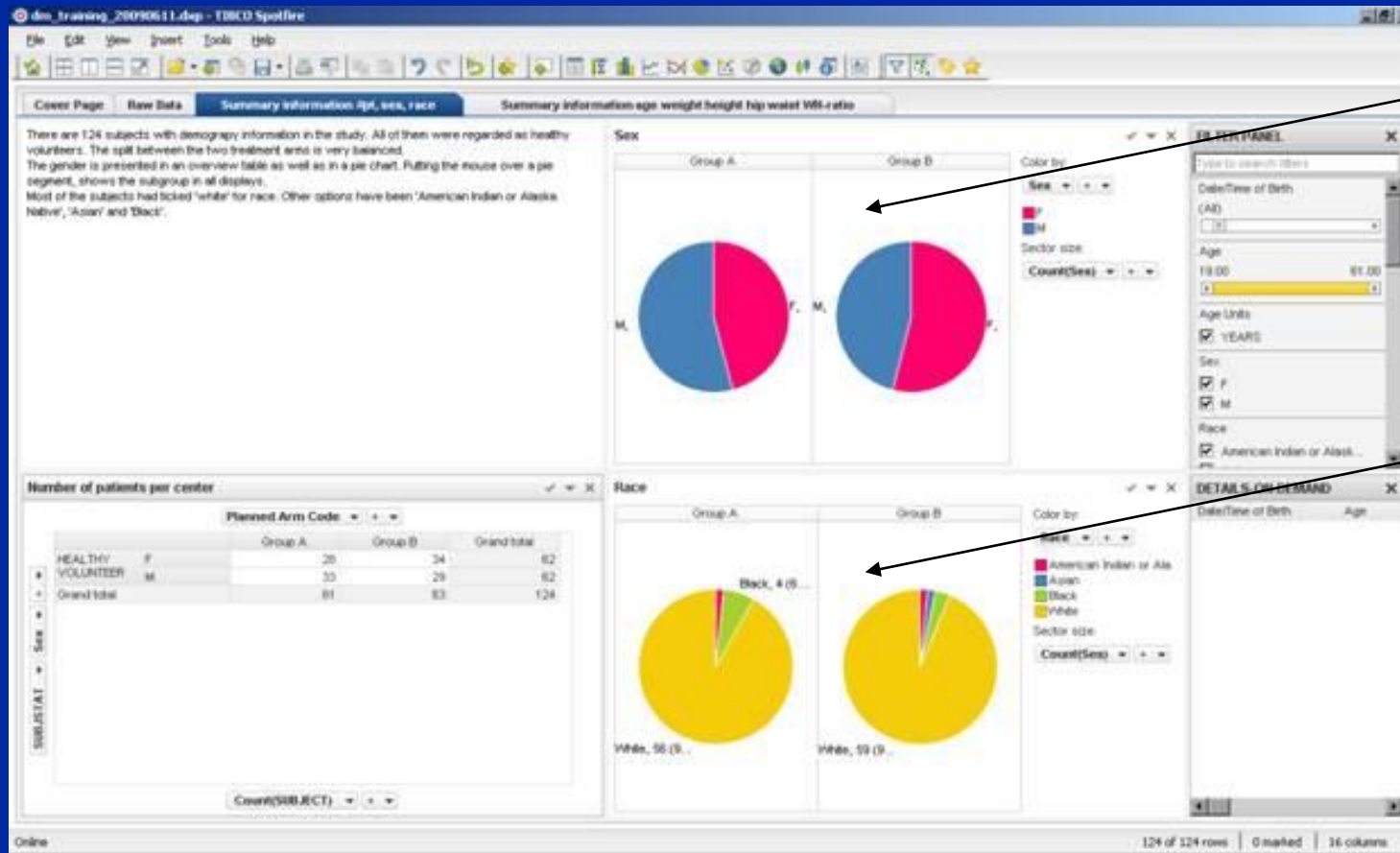
- Stable data model resulting in data sets tailored for medical data review
- Underlying principle: most of the derivations required for medical data review should be programmed up-front; examples for derivations:
 - Study day
 - Baseline calculations
 - Change from baseline
 - Flagging of lab values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

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

- 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.

TIBCO Spotfire Examples: Viewing of Entire Datasets



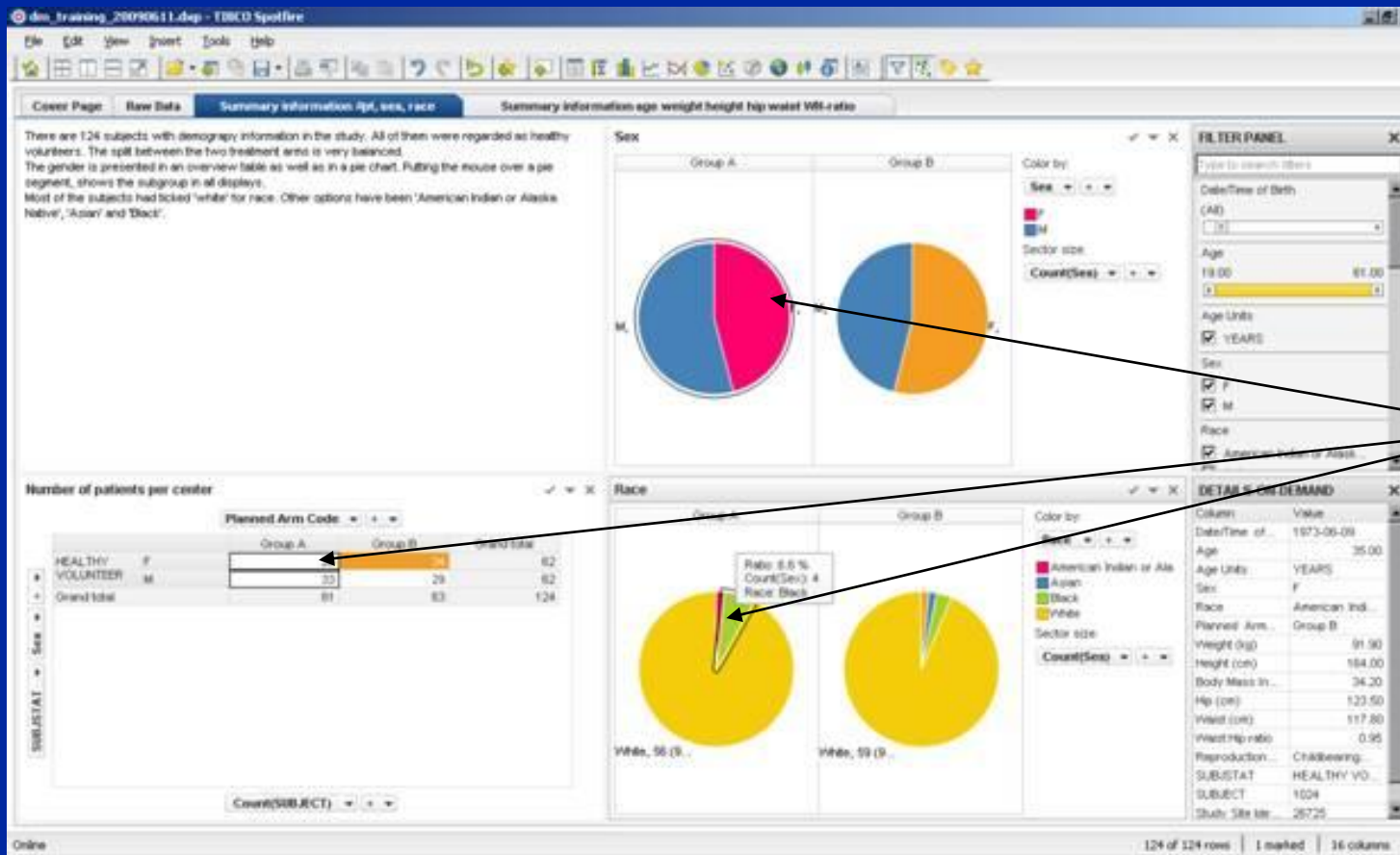
Gender Distribution

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

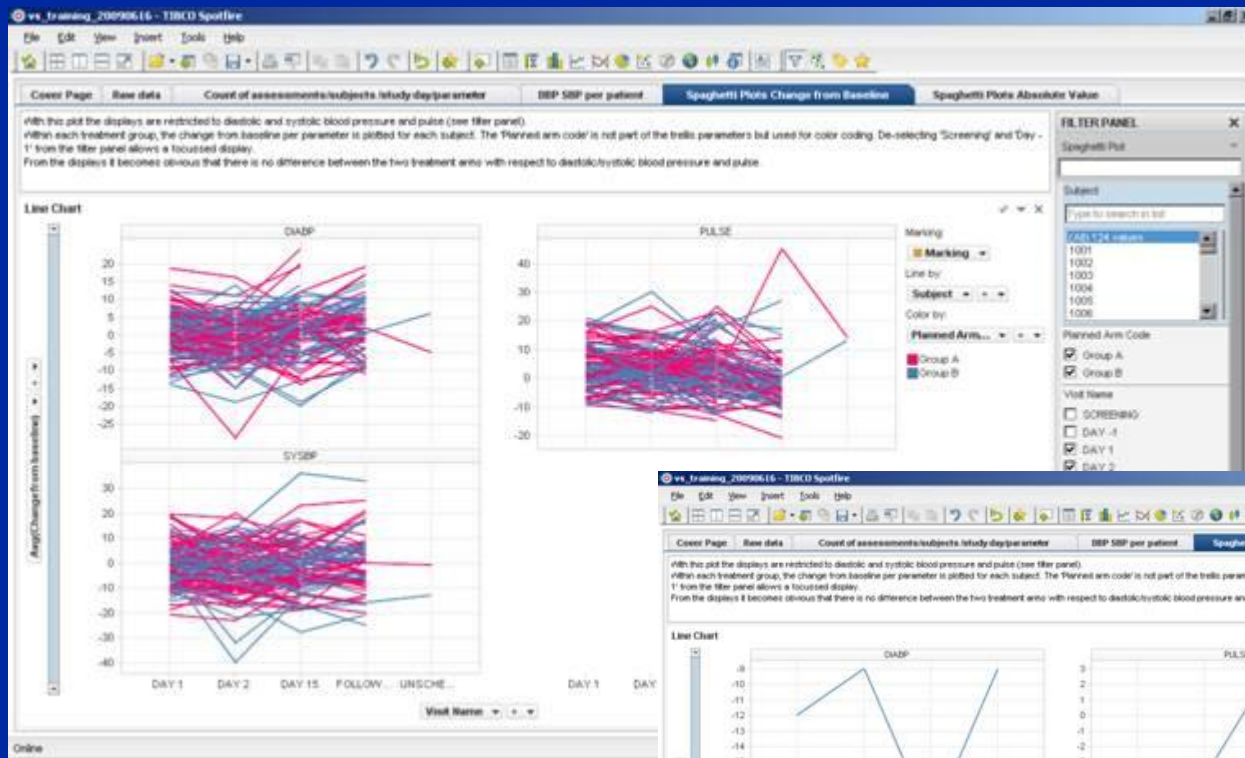
- The templates are interactive and by selecting particular components of one of the pie charts, all other visualizations on the page are updated in real time.



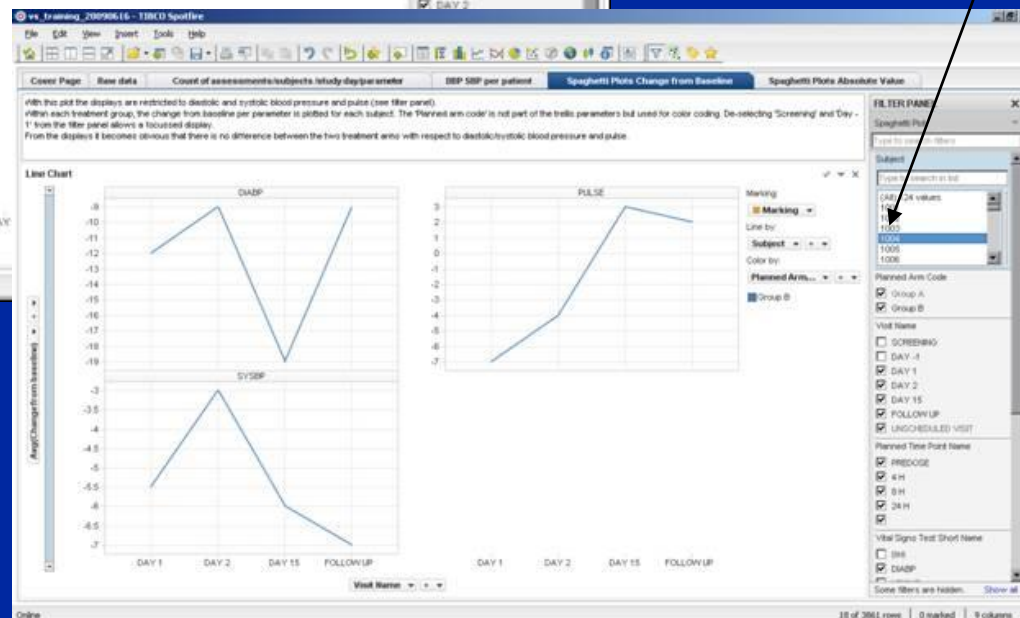
Real time update of data

TIBCO Spotfire Examples: Drill-Down to Subject Level

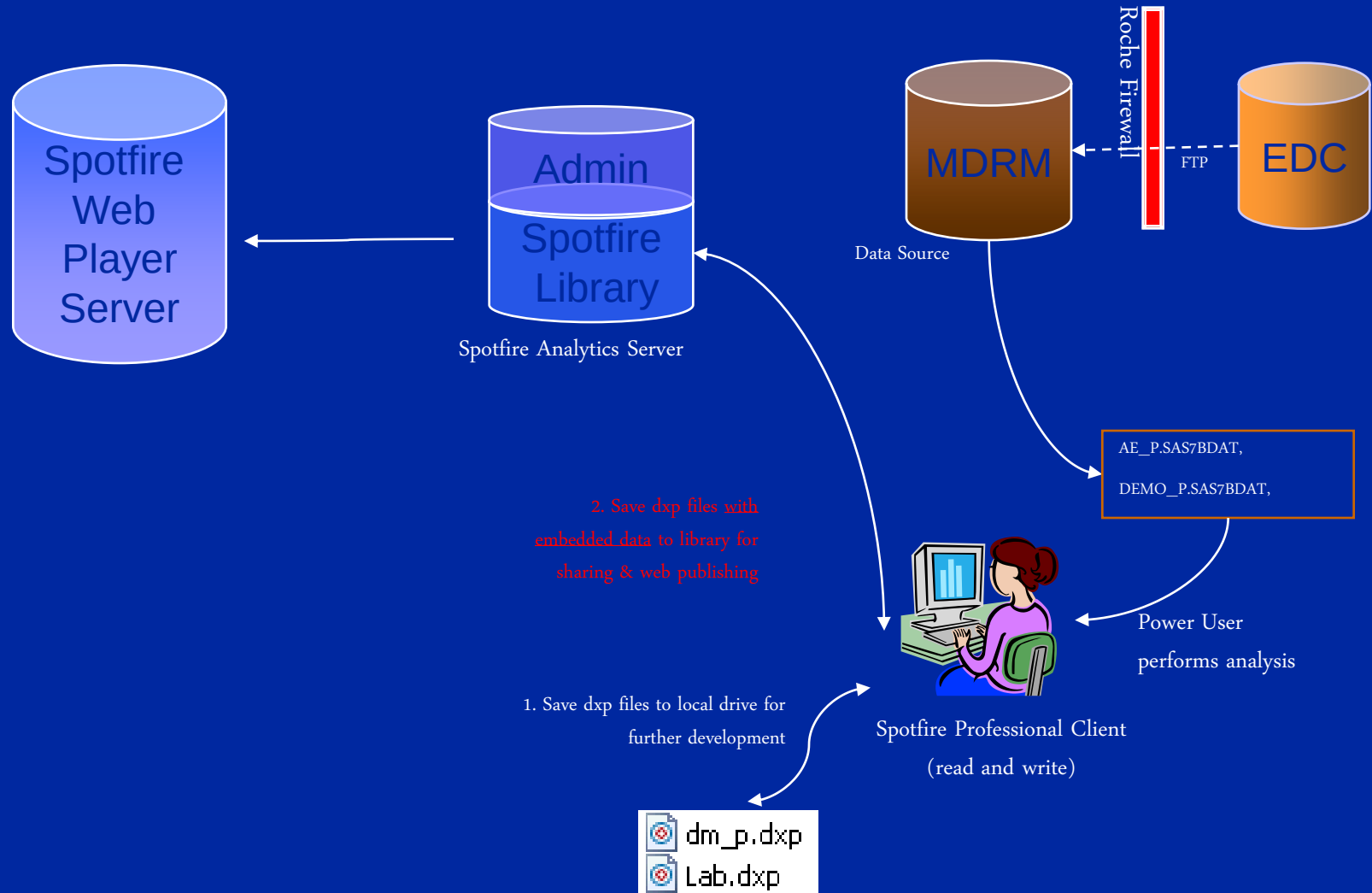
- One additional aspect is the ability to review large data sets and to drill down to subject level data.



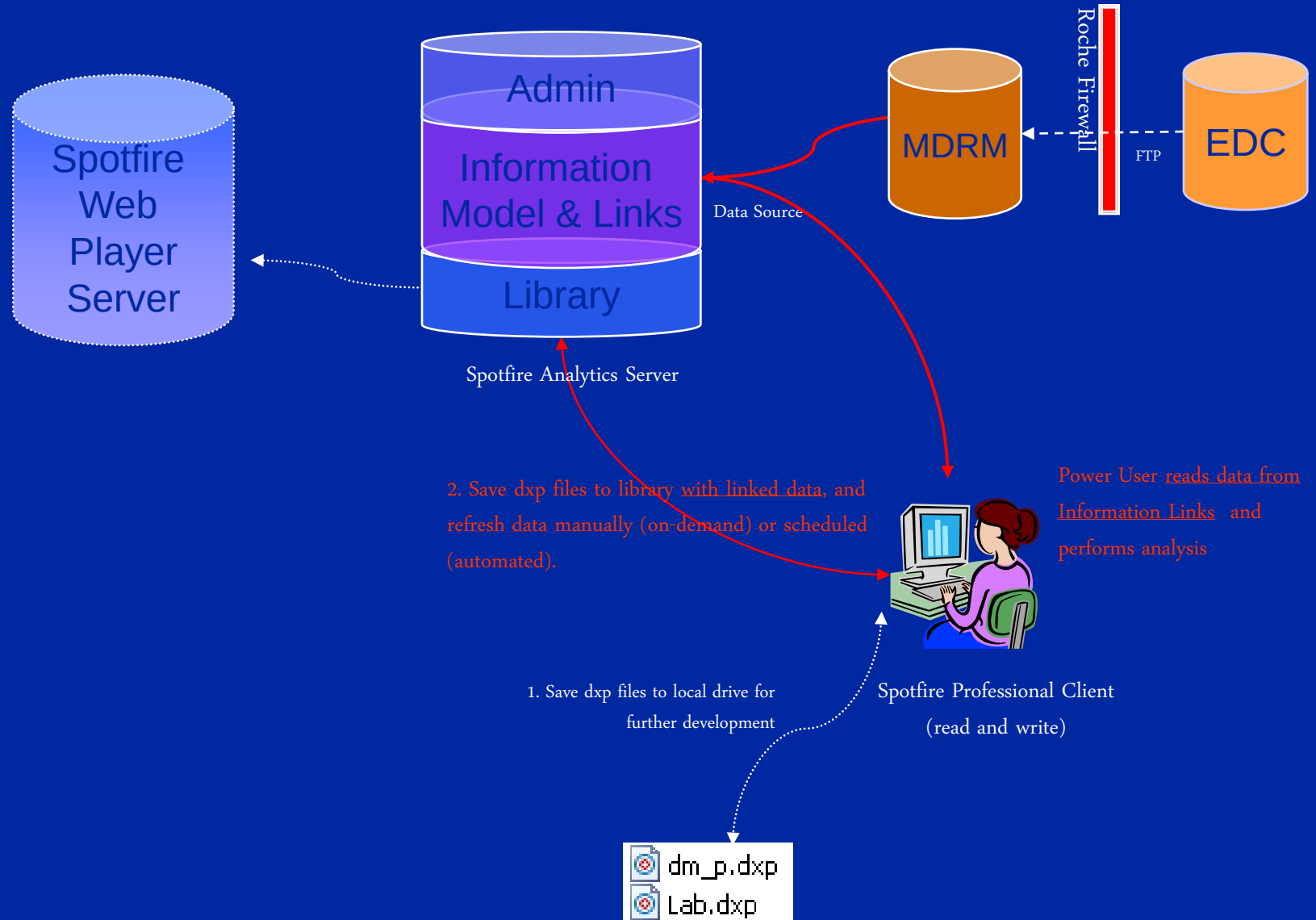
Drill-Down to Subject



Current Pilot Implementation at Roche



Planned Implementation at Roche



Acknowledgement



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Thank you very much !!!