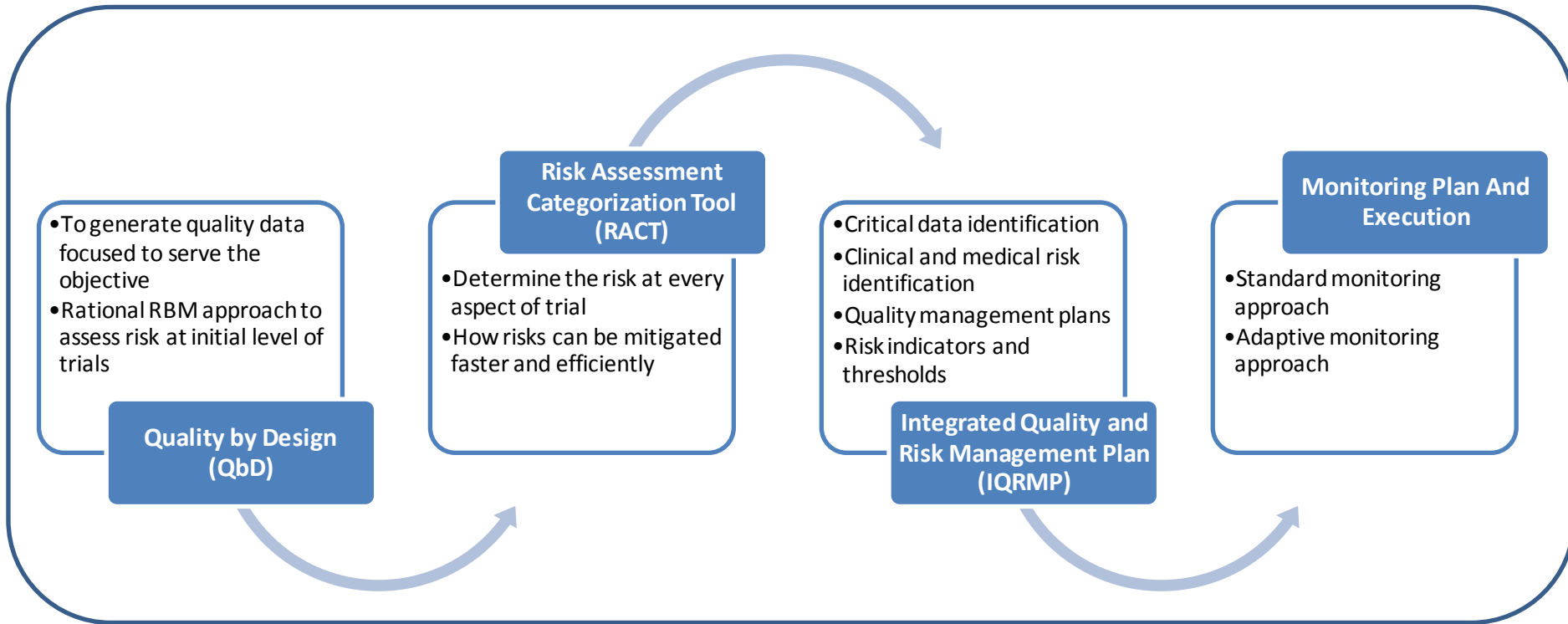


RISK BASED MONITORING THROUGH INTEGRATED CLINICAL DEVELOPMENT PLATFORM

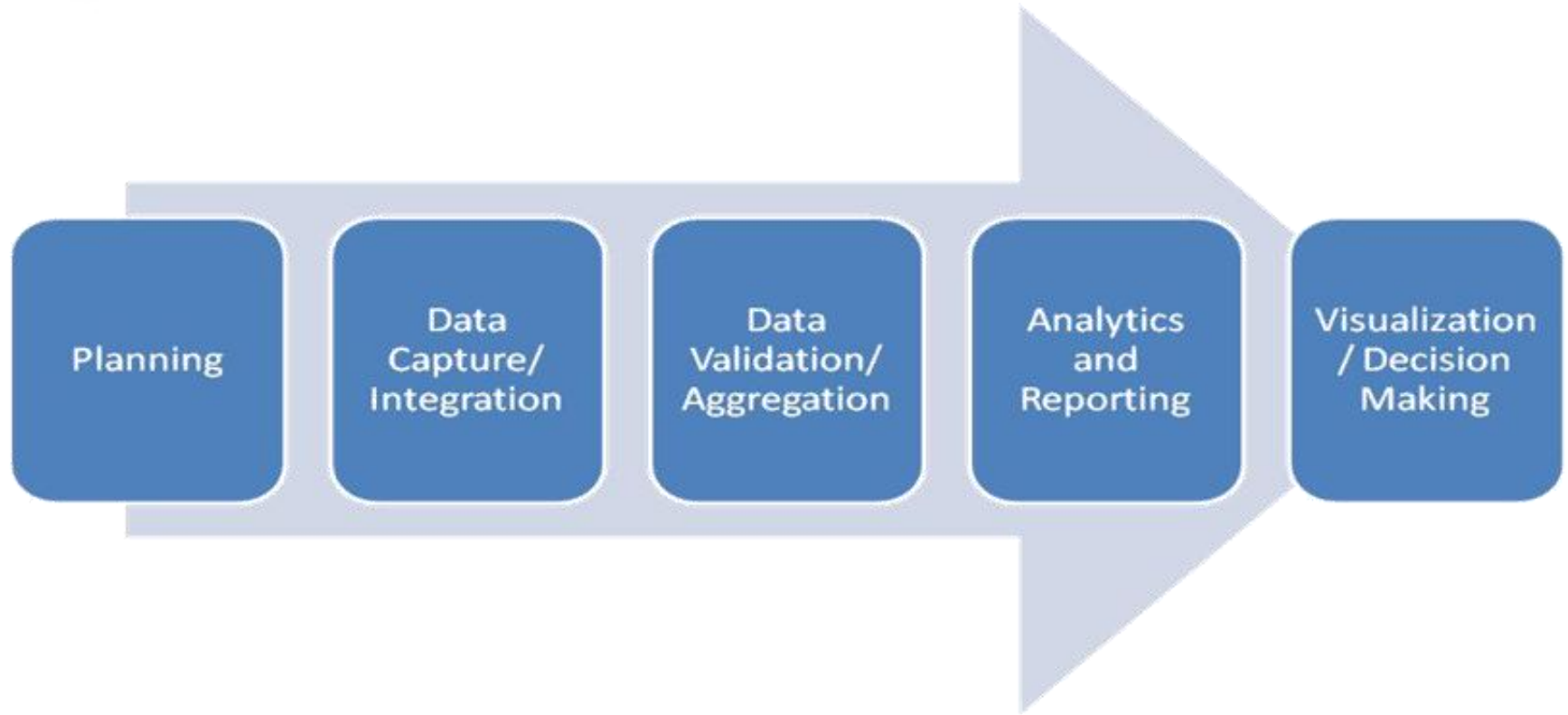
Mr. Sita Rama Swamy Peddiboyina

Mr. Jonathan Taylor



Monitoring is shifting to Risk Based Monitoring by

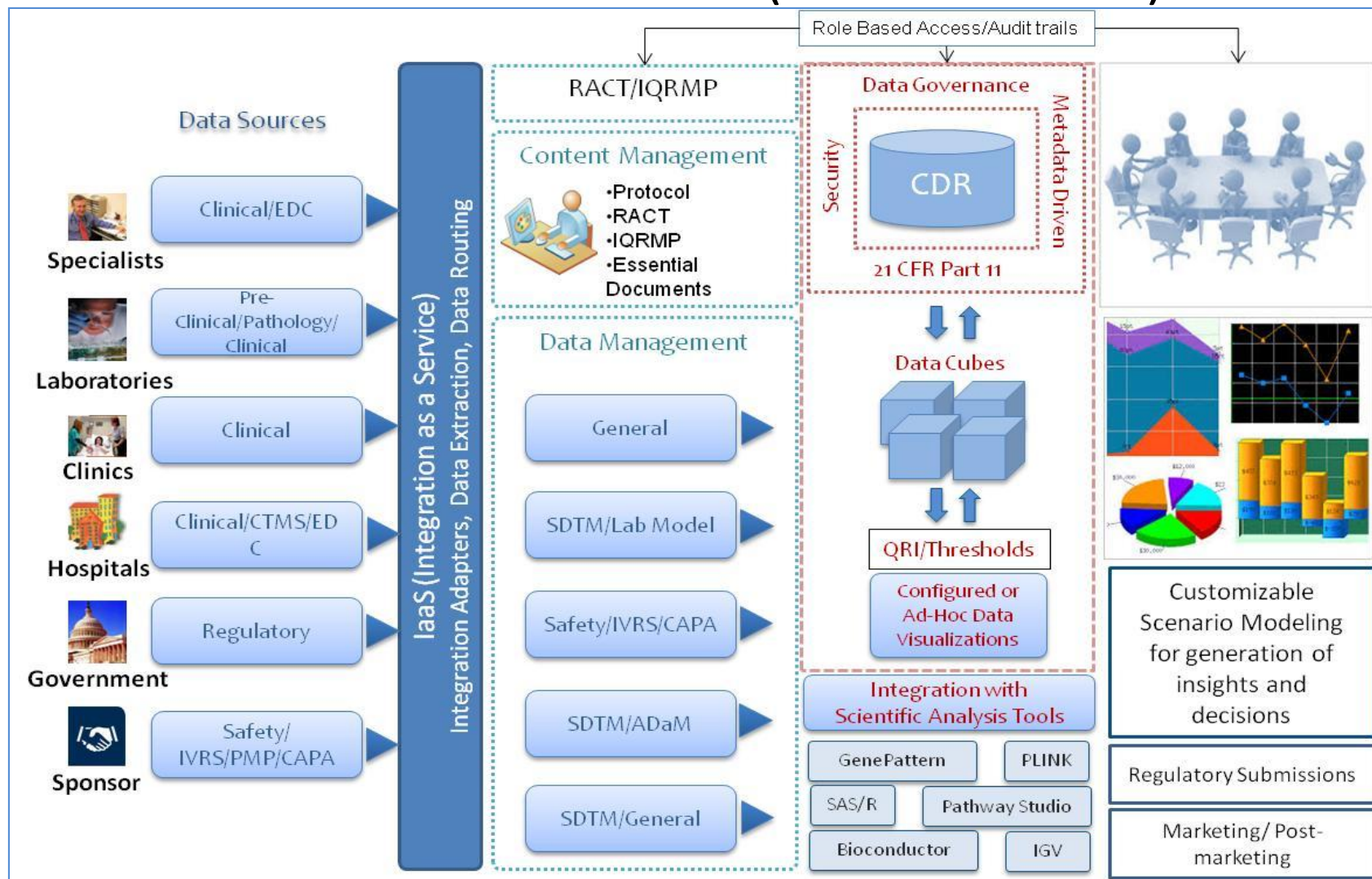
- ✓ 100% Source Data Verification (SDV) to Risk Based Focus, Source Data Review (SDR)
- ✓ More On Site Level to More Off Site and Targeted On Site Approach
- ✓ Fragmented to Centralized monitoring
- ✓ Rigid to Adaptive Approach



Basic System requirements for RBM should have ability to handle steps like

- Planning
- Data Capture/ Integration
- Data Validation/ Aggregation
- Analytics and Reporting
- Visualization and Decision Making

Integrated Clinical Development Platform (CTRenaissance) based RBM



✓ Integrated Clinical Development platform allows end to end solution for clinical drug development.

Data Sources

Specialists



Clinical/EDC



Pre-Clinical/Pathology/
Clinical

Laboratories



Clinical

Clinics



Clinical/CTMS/ED
C

Hospitals



Regulatory

Government



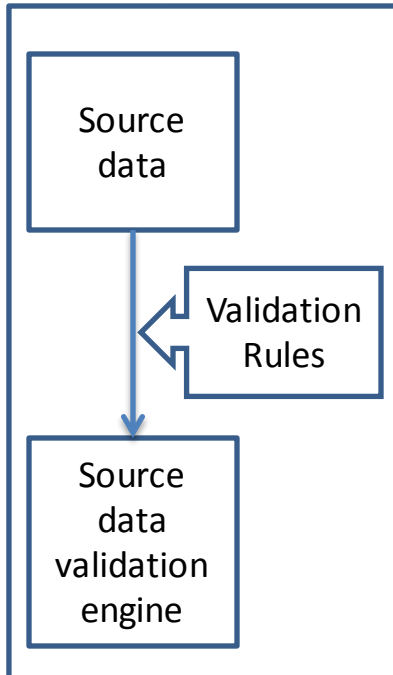
Sponsor

Safety/
IVRS/PMP/CAPA

IaaS (Integration as a Service)
Integration Adapters, Data Extraction, Data Routing

The screenshot displays the MAXISIT eXchange web application. The top navigation bar includes 'Dashboard', 'File', 'New', 'Tools', 'Process', and 'Help'. The user is logged in as 'Ramaswami P - Data Manager (Project Team)'. The main content area is titled 'Data Import wizard' and shows the 'Select Import Type' step. On the left, a 'Project Management' tree shows a hierarchy for 'MAXISIT007_DATAMANAGEMENT', with 'Metadata' expanded to show 'EDC', 'SDTM (1)', 'CTMS', 'LAB_DATA', and 'PKDATA'. A red circle highlights this 'Metadata' section. The main panel on the right shows the 'Select Import Type' step with icons for Excel, XML, Database, CSV, TSV, and XPT. A red circle highlights the 'Metadata' section in the Project Management tree. The bottom of the interface shows 'Integration Management', 'Quality Management', 'Metadata and Forms Management', and 'Study Explorer'.

✓ Integration of disparate data sources is possible to access data at a single platform from different sources like EDC tools, CTMS, Lab Data with advantage of metadata driven technology.



MAXISIT® eXchange

Ramaswami P - Data Manager (Project)

Study Info

Dashboard | File | New | Tools | Process | Help

Process Management

Project Management

MAXISNEU007_DATAMANAGEMENT

Metadata

- Edit Metadata
- Create Validation Check
- Export Metadata
- GridView Metadata
- Review Metadata
- Query Builder
- Properties
- Data Validation**
- Dependency Graph
- Re Import Data
- Relations

Mapping

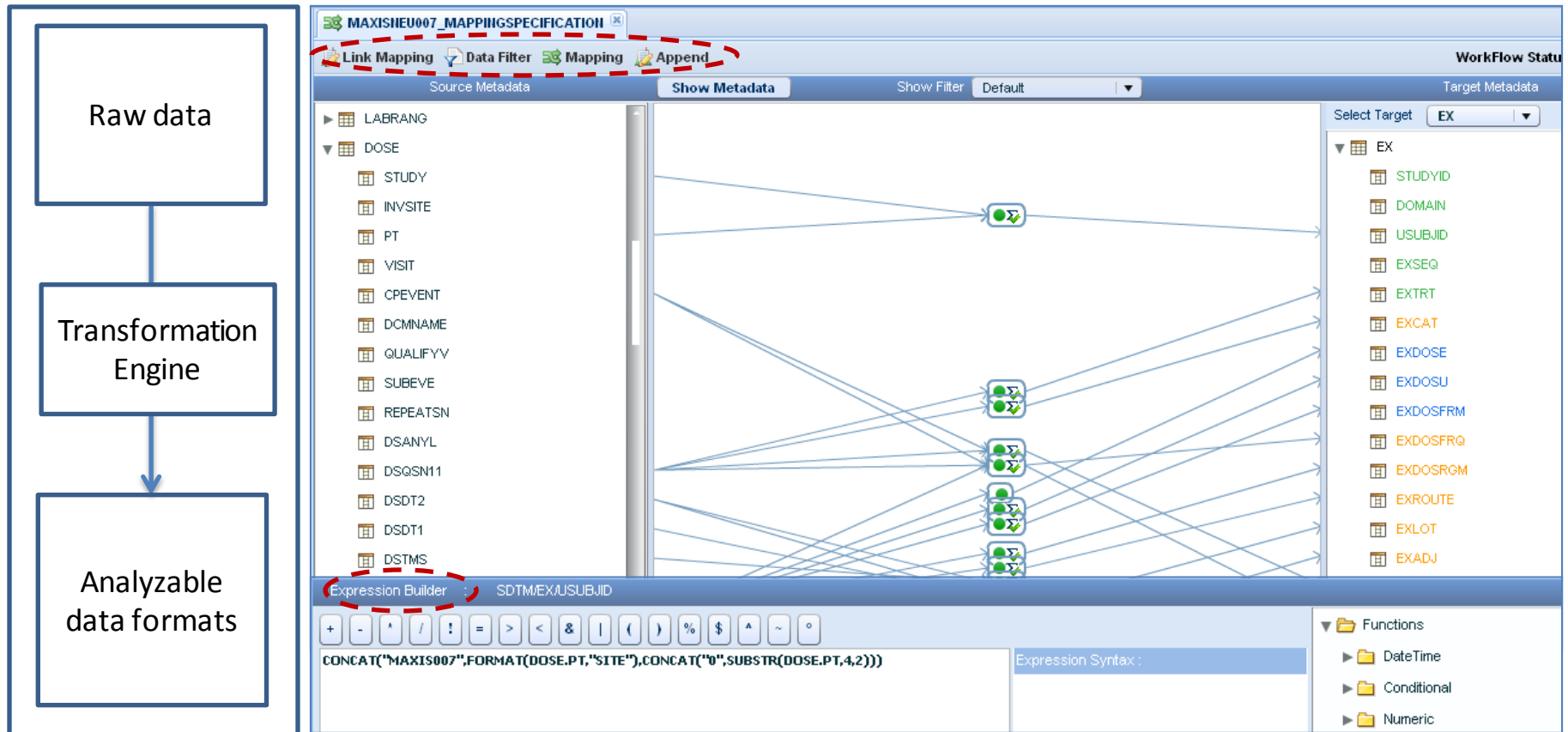
- Data Source
- In
- Out
- Data Validation
- Execution
- Schedule

Validation Rules

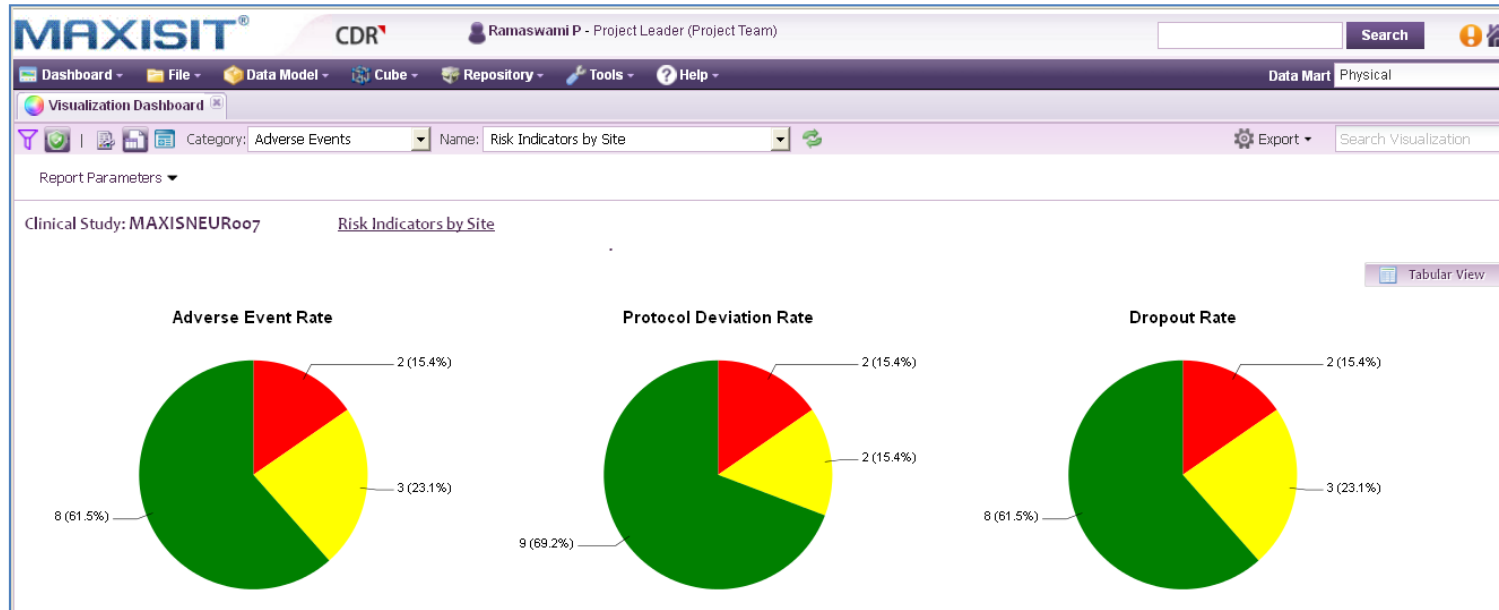
- ☐ Rule Name
- ☒ All unique key variables in each raw data set are required.
- ☒ Minimum and maximum values of selected variables.
- ☒ Check Missing values for selected variables(Required Variables).
- ☒ Check the consistency between two clinical dates.
- ☒ Check for duplicate records.
- ☐ Are there any outliers for any selected Critical variables.
- ☒ Acceptable Values(Values are one of the valid values for selected variable)
- ☐ Check for Negative Values.
- ☐ Character variables(text) exceed 200 bytes.

Name	Record	Variables	Values	RuleID	Message		
BIOLAB	1	LVALUE2		CTR0046	LVALUE2 is missing		
BIOLAB	5	LVALUE2		CTR0046	LVALUE2 is missing		
BIOLAB	28	LVALUE2		CTR0046	LVALUE2 is missing		
BIOLAB	30	LVALUE2		CTR0046	LVALUE2 is missing		
BIOLAB							
BIOLAB		VISIT	CPEVENT	LPARM	LUNIT	LVALUE2	LABQSN1
BIOLAB	1	BASELINE	PSA	NG/ML			
BIOLAB	1	BASELINE	CA-125	IU/ML	58		
BIOLAB	1	BASELINE	OTHER	U/ML	2584.4	CA 19-9	
BIOLAB	1	BASELINE		NG/ML	4.6	CEA	
BIOLAB	9	END OF CYCLE 1	PSA	NG/ML			
BIOLAB	9	END OF CYCLE 1	CA-125	IU/ML	16		
BIOLAB	9	END OF CYCLE 1	OTHER	NG/ML	4.3	CEA	
BIOLAB	9	END OF CYCLE 1		U/ML	3638.7	CA 19-9	
BIOLAB	1	BASELINE	OTHER	NG/ML	69979	ALPHA FETOPR...	
BIOLAB	9	END OF CYCLE 1	OTHER	NG/ML	161776	ALPHA FETOPR...	

- ✓ Source data validation can be performed at application level before transformation of data
- ✓ Data validation engine allows customized rule setup for source data enabling to validate required data fields for missing data, duplicate records, data outliers, and inconsistent data. .



- ✓ Data from different data sources is transformed to standard or proprietary analyzable formats.
- ✓ This allows analytical engine to analyze different data at single platform
- ✓ Expression builder allows users to derive target variables through predefined functions



SA	STUDYID	SITEID	ENROLLED	AE Count	Adverse Event Rate	Protocol Deviation	Protocol Deviation	Dropout Count	Dropout Rate	SAE Count
	MAXISNEUR007	7802	12	3	.25	0	0	1	.08	0
	MAXISNEUR007	7825	2	0	0	0	0	0	0	0
	MAXISNEUR007	7822	19	13	.68	0	0	0	0	0
	MAXISNEUR007	7824	18	0	0	0	0	2	.11	0
	MAXISNEUR007	7815	24	20	.83	1	.04	3	.13	0
	MAXISNEUR007	7813	7	1	.14	0	0	1	.14	0
	MAXISNEUR007	7823	28	14	.5	1	.04	1	.04	0
	MAXISNEUR007	7814	25	33	1.32	0	0	0	0	0
	MAXISNEUR007	7808	10	10	1	2	.2	0	0	1
	MAXISNEUR007	7809	2	5	2.5	4	2	0	0	0
	MAXISNEUR007	7818	4	10	2.5	2	.5	0	0	0
	MAXISNEUR007	7805	12	2	.17	1	.08	0	0	0
	MAXISNEUR007	7826	1	1	1	0	0	0	0	0

- ✓ User friendly and role based dashboard allows users to have overview of risk indicators.
- ✓ Dashboard allows user to drilldown further to understand the risk criteria in detail.

Risk Assessment and Categorization Tool (RACT)

MAXISIT® CDR | Ramaswami P - Project Leader (Project Team) | Search | Data Mart: Physical

Dashboard | File | Data Model | Cube | Repository | Tools | Help | Visualization Dashboard | RACT Template

Save | Monitoring Activity | IQRMP | Workflow | Publish

Overall Risk Level ▲ 52.50 Medium | List View | Summary View

RACT Version 1.0 on 08/08/2014

1 Safety Determine any known risks for subject safety | Total Category Risk is 27 | Weightage 1

2 Study Phase Factor the risks inherent in the study phase into the trial | Total Category Risk is 18 | Weightage 1

3 Complexity Determine how the | Overall Risk Level ▲ 52.50 Medium | List View | Summary View

4 Subject Pop Determine whether

5 Technology What level of techn

6 Data Collect Assess the integrity

7 Endpoints Determine if the m

8 Organizatio Determine any pos

9 Investigatio Determine any risks

10 IP Logistics Determine risk invo

11 Blinding Determine to what

1 Safety Determine any known risks for subject safety

L1 Question Per the Medial Surveillance Team (MST) Chair with Medical Leader confirm what is the safety risk to the subject?

Considerations Identified risks from the Medical Surveillance Team which have predetermined rules for determining safety risk with confirmation from the Medical Leader

Impact 3 Probability 3 Detectability 3

Program/protocol risk Protocol

Risk level rationale

Functional Plan(s) Impacted Site Monitoring Plan, Medical Monitoring Plan, Safety Plan, Statistical Data Review Plan, Training

High risk(Considerations) Identified risks per MST

Medium risk(Considerations) Potential risks per MST

Low risk(Considerations) no potential or identified risks

Total Category Risk is 27 | **Weightage** 1 | **Total category Risk Score** 27

- ✓ RACT allows early risk assessment for trial or program.
- ✓ Easy to use interface and highly validated RACT algorithm allows risk levels for the trial.
- ✓ Risk questions can be added and deleted
- ✓ Program or Protocol level of risk can be set in the RACT
- ✓ Plans impacted by specific risk can be selected in the RACT

Integrated Quality and Risk Management Plan (IQRMP)

Reference inputs from RACT are pre-populated in specific plan which can be edited to set the risk indicators and thresholds

Data sources can be defined to access the specific data

Safety Plan
Describes how pharmacovigilance/drug safety will manage safety risks related to a product Repository IQRMP Safety plan

Per the Medial Surveillance Team (MST) Chair with Medical Leader confirm what is the safety risk to the subject?

Source: EDC

Activities: Adverse Events Sub Activities: Adverse Events reporting

Site Authority: Metadata Manager, Project Leader, Project Physician

Threshold: LOW: less than or equal 1, MEDIUM: in between 1 2, HIGH: greater than 2

Escalation Condition: after 12 Hours, after 15 Hours, after 24 Hours

Escalation To: Metadata Manager, Project Leader, Project Physician, MdR Admin, Metadata Manager, Project Leader, Dashboard Administrator, Data Manager, MdR Admin

Actions(s): no action, Call site, Visit site

Roles to be notified: Project Leader

Risk levels thresholds can be set for Low, Medium and High for risks

Escalation thresholds and escalation levels can be set for Low, Medium and High for risks

Alert notification settings are set with the thresholds

Action items can be defined in IQRMP for risk level alerts

Application of Thresholds on Report Parameters

Dashboard - File - Data Model - Cube - Repository - Tools - Help - Data Mart Physical

Visualization Dashboard - Reports Portfolio Manager - Edit Risk Indicators by Site

Data Grid Designer

Table

- STUDYID
- SITEID
- ENROLLED
- AECOUNT
- Adverse Event Rate
- DVCOUNT
- Protocol Deviation Rate
- DSCOUNT
- Dropout Rate
- SAE Count

Properties

Name	Value
text	Adverse Event Rate
resizable	true
name	AERATE
dataIndex	AERATE
hasDrillDown	false
category	Safety
riskIndicator	MAXISNEUR007/Safety Plan/...

Data Grid Settings

Query Design - Data Grid Design - Report Level Metadata

Header text

STUDYID	SITEID	ENROLLED	AECOUNT	AERATE	DVCOUNT	DVRATE	DSCOUNT	DSRATE	SAECOUNT
MAXISNEUR007	7813	7	1	.14	0	0	1	.14	0
MAXISNEUR007	7808	10	10	1	2	.2	0	0	1
MAXISNEUR007	7822	19	13	.68	0	0	0	0	0
MAXISNEUR007	7825	2	0	0	0	0	0	0	0
MAXISNEUR007	7815	24	20	.83	1	.04	3	.13	0
MAXISNEUR007	7823	28	14	.5	1	.04	1	.04	0
MAXISNEUR007	7802	12	3	.25	0	0	1	.08	0
MAXISNEUR007	7818	4	10	2.5	2	.5	0	0	0
MAXISNEUR007	7805	12	2	.17	1	.08	0	0	0
MAXISNEUR007	7822	19	13	.68	0	0	0	0	0
MAXISNEUR007	7805	12	2	.17	1	.08	0	0	0
MAXISNEUR007	7809	2	5	2.5	4	2	0	0	0
MAXISNEUR007	7808	10	10	1	2	.2	0	0	1
MAXISNEUR007	7826	1	1	1	0	0	0	0	0
MAXISNEUR007	7826	1	1	1	0	0	0	0	0
MAXISNEUR007	7815	24	20	.83	1	.04	3	.13	0
MAXISNEUR007	7802	12	3	.25	0	0	1	.08	0
MAXISNEUR007	7824	18	0						
MAXISNEUR007	7823	28	14						
MAXISNEUR007	7814	25	33						
MAXISNEUR007	7814	25	33						
MAXISNEUR007	7824	18	0						
MAXISNEUR007	7813	7	1						
MAXISNEUR007	7825	2	0						
MAXISNEUR007	7809	2	5						

User Note

Risk Category as per RACT

Risk Indicator based on RACT

From: ctrpro@ct-renaissance.com [<mailto:ctrpro@ct-renaissance.com>]

Sent: Monday, September 29, 2014 2:11 PM

To: ramaswami@int.maxis.com

Subject: Alert Notification from CTRenaissance, Risk Based Monitoring Platform

CTRENAISSANCE
Powered by MaxisIT

Dear Ramaswami P,

Alert Notification from CTRenaissance, Risk Based Monitoring platform for Study MAXISNEUR007.

Last data ported on 2014-08-03.

Risk Indicator	Risk Level	No. Of Sites	Action
Does The Phase Of The Trial Increase The Risk?	High	2	call Visits
	Medium	2	co-ordinate With Project Team Or Call Them
	Low	9	no Action
Per The Medial Surveillance Team (mst) Chair With Medical Leader Confirm What Is The Safety Risk To The Subject?	High	2	visit Site
	Medium	3	call Site And Action
	Low	8	call Site
Does The Protocol Require Any Complex Or Uncommon Procedures Beyond The Usual Standard Of Care?	High	2	visit Site
	Medium	3	co-ordinate With Project Team Or Call Them
	Low	8	no Action

Please review the reports for further details on your Dashboard.

Sincerely,
 CT-Renaissance
 MaxisIT Inc.

- ✓ Whenever thresholds are exceeded, defined users will get email notification .
- ✓ Alert also shows the date of latest data ported.
- ✓ Alert provides the action items listed in the threshold settings

Type of Monitoring **Category** **Activity** **SubActivity** **StudyId:**

Central Safety Adverse Events Adverse Events reporting MAXISNEUR007

Issue Identified	Risk Level	Activity Date	Action	Status	Comments	Site Id	Subject Id
Does the Phase of t...	Low	09/25/2014 2:56 AM	No Action	Pending	Risk observed in 1 Site(s)		
Does the Phase of t...	Medium	09/25/2014 2:56 AM	Co-ordinate wit...	Pending	Risk observed in 0 Site(s)		

Dashboard File Data Model Cube Repository Tools Help Data Mart Physical

board RACT Template IQRMP for MAXISNEUR007 Reports Portfolio Manager Edit Demographic Characteristics Monitoring Activity Report for MAXISNEUR007 Monitoring Activity Repo

Type Of Monitoring OnSite

Category

- Safety
- Study Phase
- Complexity
- Subject Population
- Technology
- Data Collection

Risk Indicators

- Low
- Medium
- High
- Undefined

From **To**

Generate Report Publish Report

Export as

Issue Identified	Risk Level	Activity Date	Action	Status	Comments	Site Id	Subject Id
AE rate very high	High	08/08/2014 8:24 AM	visit site	Pending	visit scheduled on 11th aug	7818	
High Drop out rate	High	08/08/2014 7:46 AM	Visit Site	InProgress	Visit scheduled on 10th Aug	7818	
High Risk at 7809	High	08/08/2014 7:46 AM					

Type Of Monitoring **Category** **Activity** **SubActivity** **StudyId:**

Select Select Select Select MAXISNEUR007

Site Id Subject Id

Issue Identified

Risk Level: Select Activity Date

Action

Status: Select

Comments

Save IssueLog Cancel

- ✓ Monitoring interface allows user to access the reports applying multiple filters like risk category, risk level.
- ✓ Onsite monitoring observations can be recorded and issues can be logged and exported in portable document and Excel formats.

STUDYID	SITEID	ENROLLED	AE Count	Adverse Event Rat	Protocol Deviation	Protocol Deviation	Dropout Count	Dropout Rate	SAE Count
MAXISNEUR007	7800	10	10	1	2	.2	0	0	1
MAXISNEUR007	7800	Demographics	5	2.5	4	2	0	0	0
MAXISNEUR007	7820	Laboratory Test Reports	0	0	0	0	2	.11	0
MAXISNEUR007	7800	Adverse Events	2	.2	1	.08	0	0	0
MAXISNEUR007	7820	Concomitant Medications						0	0
MAXISNEUR007	7810	Medical History						0	0
MAXISNEUR007	7820	Protocol Deviations						.13	0
MAXISNEUR007	7810	Vital Signs						.04	0
MAXISNEUR007	7820							.14	0
MAXISNEUR007	7813	/						.08	0
MAXISNEUR007	7802	12							

Clinical Study: MAXISNEUR007

Number of Subjects with Adverse Events by Severity across Treatment Group

System Organ Class	Preferred term	Severity	MAXN007 2 mg (N=1)	MAXN007 6 mg (N=2)	Placebo (N=1)	Total (N=10)
Nervous system disord...	Balance disorder	MODERATE		1 (50.00)		1 (10.00)
	Cognitive disorder	MILD			1 (100.00)	1 (10.00)
	Headache	MILD	1 (100.00)		1 (100.00)	2 (20.00)
		MODERATE		1 (50.00)		1 (10.00)
	Transient ischaemic attack	MODERATE		1 (50.00)		1 (10.00)
Metabolism and nutrit...	Fluid retention	MILD			1 (100.00)	1 (10.00)
Psychiatric disorders	Insomnia	SEVERE		1 (50.00)		1 (10.00)

- ✓ Reports can be drilled down to multiple levels to understand data in detail.
- ✓ User can see data to subject level through drill down functionality.

Report Drill Down (Continued)

Clinical Study: MAXISNEUR007

Subject Level Data

Header text

STUDYID	DOMAIN	USUBJID	SUBJID	SITEID	SEX	AGE	TRTGRP	AGEGRP
MAXISNEUR007	ADSL	MAXISNEUR007/E7808004	E7808004	7808	M	68	MAXN007 6 mg	65-85

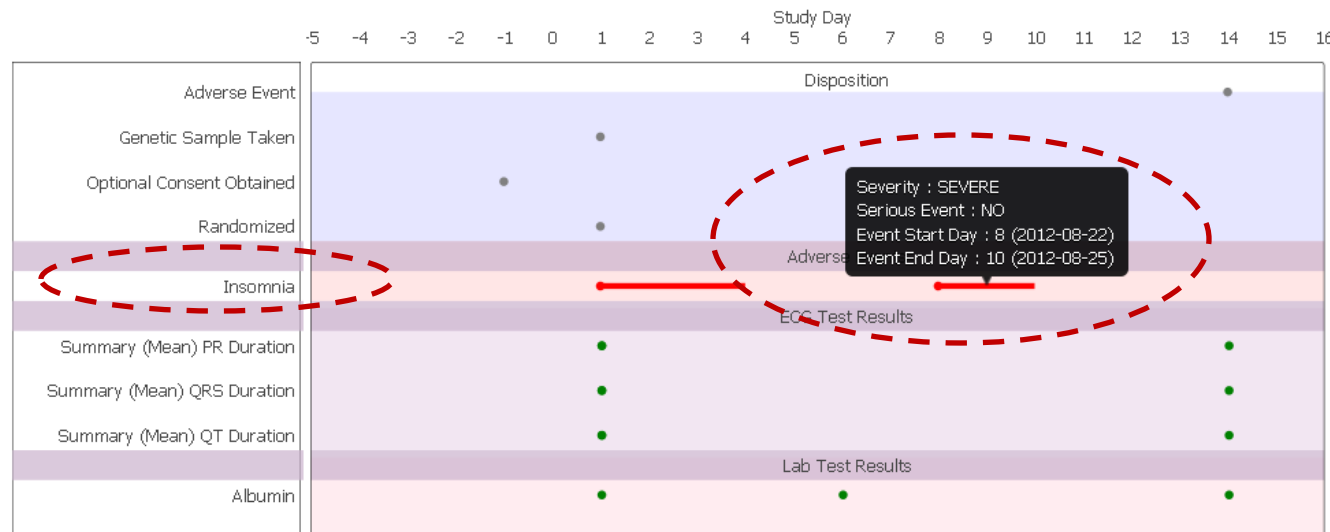
Graphical Patient Profile

Timeline Graph

Clinical Study : MAXISNEUR007 - Risk Indicators by Site » Number of Subjects with Adverse Events by Severity across Treatment Group » Subject Level Data

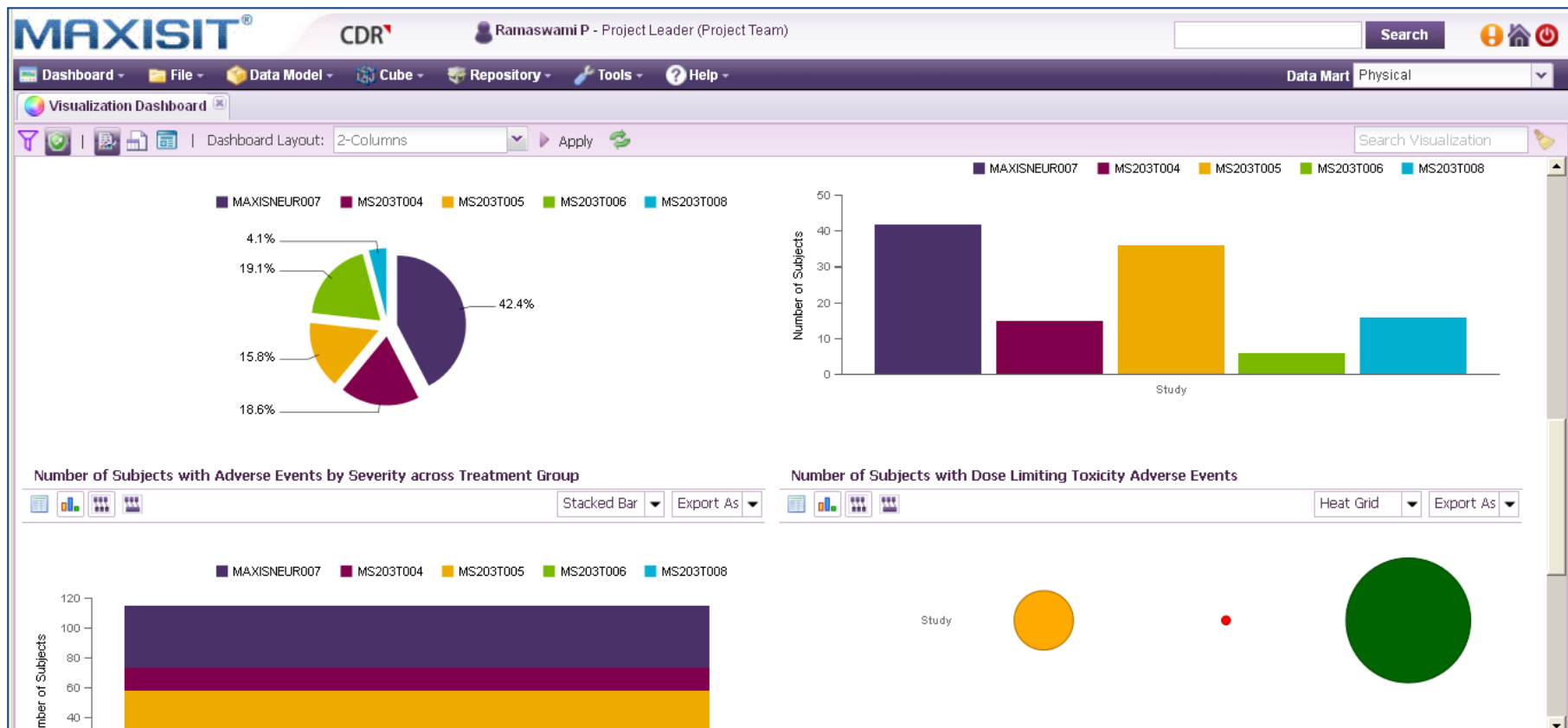
Graphical Patient Profile of Subject : MAXISNEUR007/E7808004

Demographics, Medical History Reported



Demographics	
Subject Id	MAXISNEUR007/E7808004
Arm	MAXN007 6 mg
Race	WHITE
Gender	M
Medical History Reported	
Asthma, Cognitive disorder, Dementia Alzheimer's type, Hypercholesterolaemia, Impaired fasting glucose, Nephrolithiasis, Seasonal allergy	
Context Information	
Property	Value
Dictionary-Derived Term	Insomnia
Severity	SEVERE
Serious Event	NO

- ✓ Drill down to graphical patient profile enables end user to understand subject level data at a glance.



Customizable role based dashboards enable users to understand multi level data analysis at a glance.

A word cloud of various features and services offered by MaxisIT. The words are arranged in a circular pattern, with 'MaxisIT' at the top center. Other prominent words include 'SourceDataValidation', 'Compliance', 'Analytics', 'Reports', 'RoleBasedDashboard', 'DataIntegration', 'SingleSignOn', 'Monitoring', 'Thresholds', 'WebBased', 'RiskAssessment', and 'DataAggregation'. The words are in different colors (red, orange, yellow, black) and orientations (vertical, horizontal, diagonal).

SourceDataValidation
Compliance
Analytics
Reports
RoleBasedDashboard
DataIntegration
SingleSignOn
Monitoring
Thresholds
WebBased
RiskAssessment
DataAggregation
MaxisIT

MaxisIT® builds and delivers out of the box end to end solution for efficient risk based monitoring allowing business to stay agile and lean while making better and informed business decisions that will allow them to achieve faster and quality clinical drug development compliant to regulatory and assured cost savings.



Contact Us @

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