Janus Clinical Trials Repository: Modernizing the Review Process through Innovation

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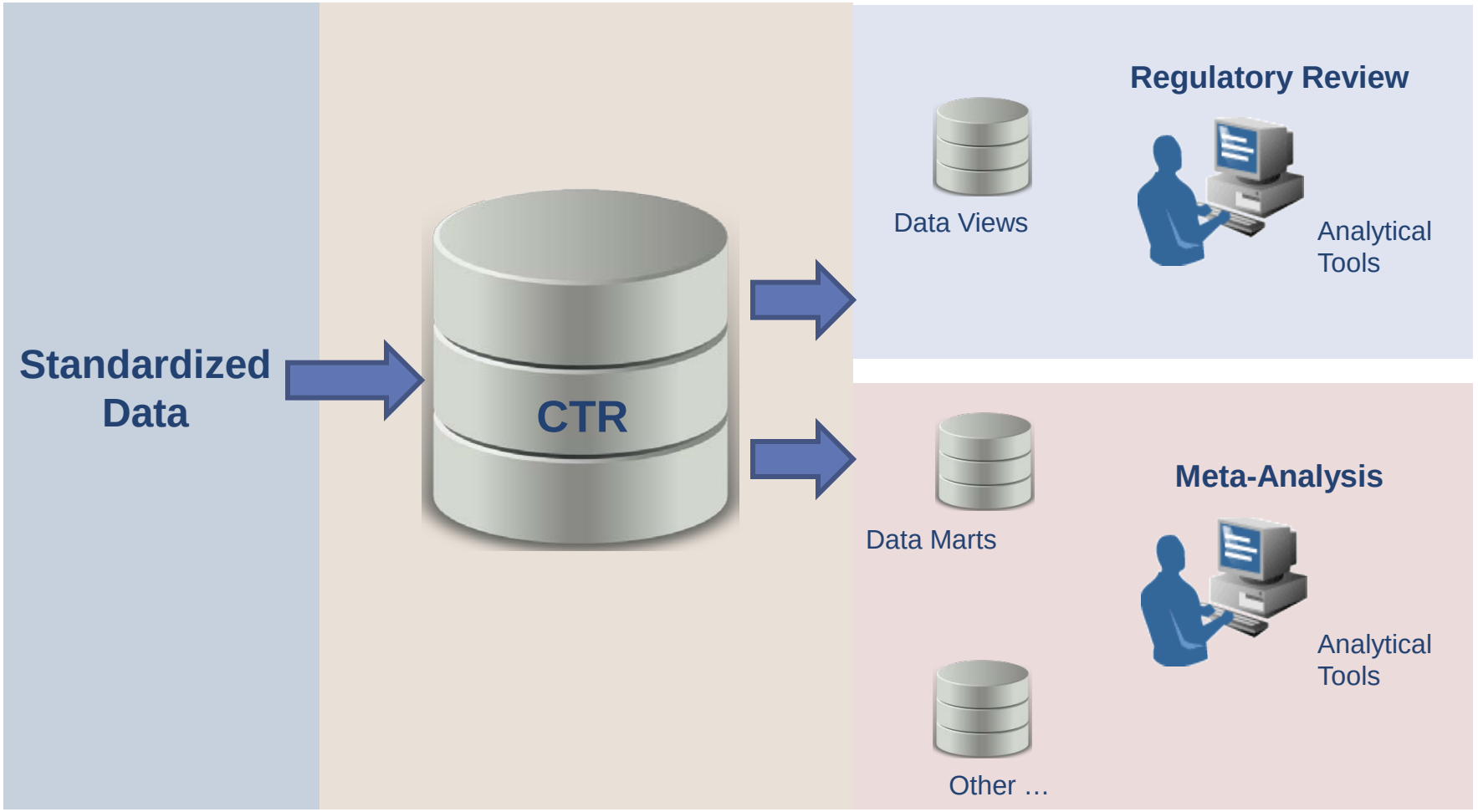
Janus Clinical Trials Repository (CTR)



Janus Clinical Trials Repository

- Supports automated extraction, transformation, loading, management, and reviewer access to standardized clinical trials data to support the regulatory review of therapeutic biologic and drug products
- Incorporates data marts designed to address specific needs
- Enables queries to be run using various analytic tools from these data marts to meet individual reviewer needs
- Leverages pre-specified analysis scripts and analytic tools

CTR is Large Data

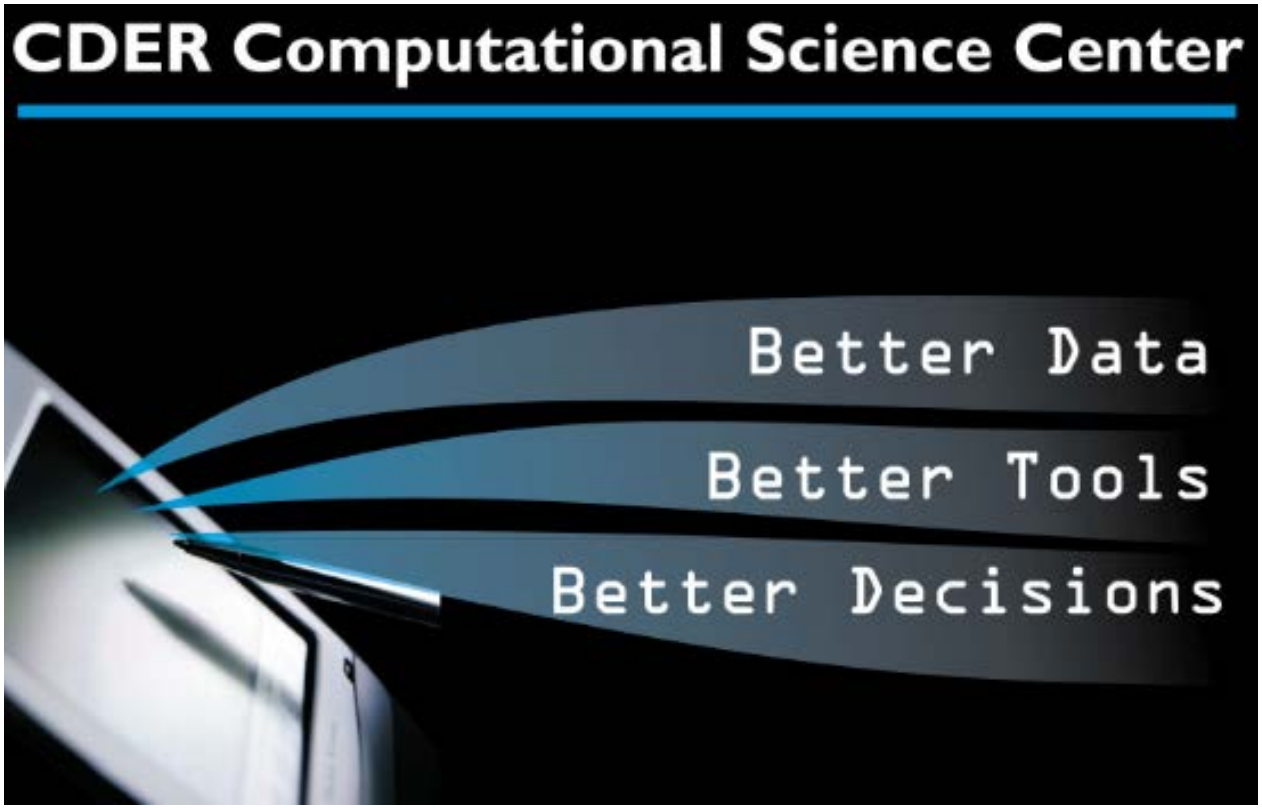
- CTR is designed to handle large data-sets
  - Is expected to grow into a very large data warehouse with many data marts.
  - Expected to grow by a few TB's every year

- CTR primarily handles:
  - Structured data
  - Low Velocity (~600 applications a year)
  - Analysis and reporting requirements are in real-time

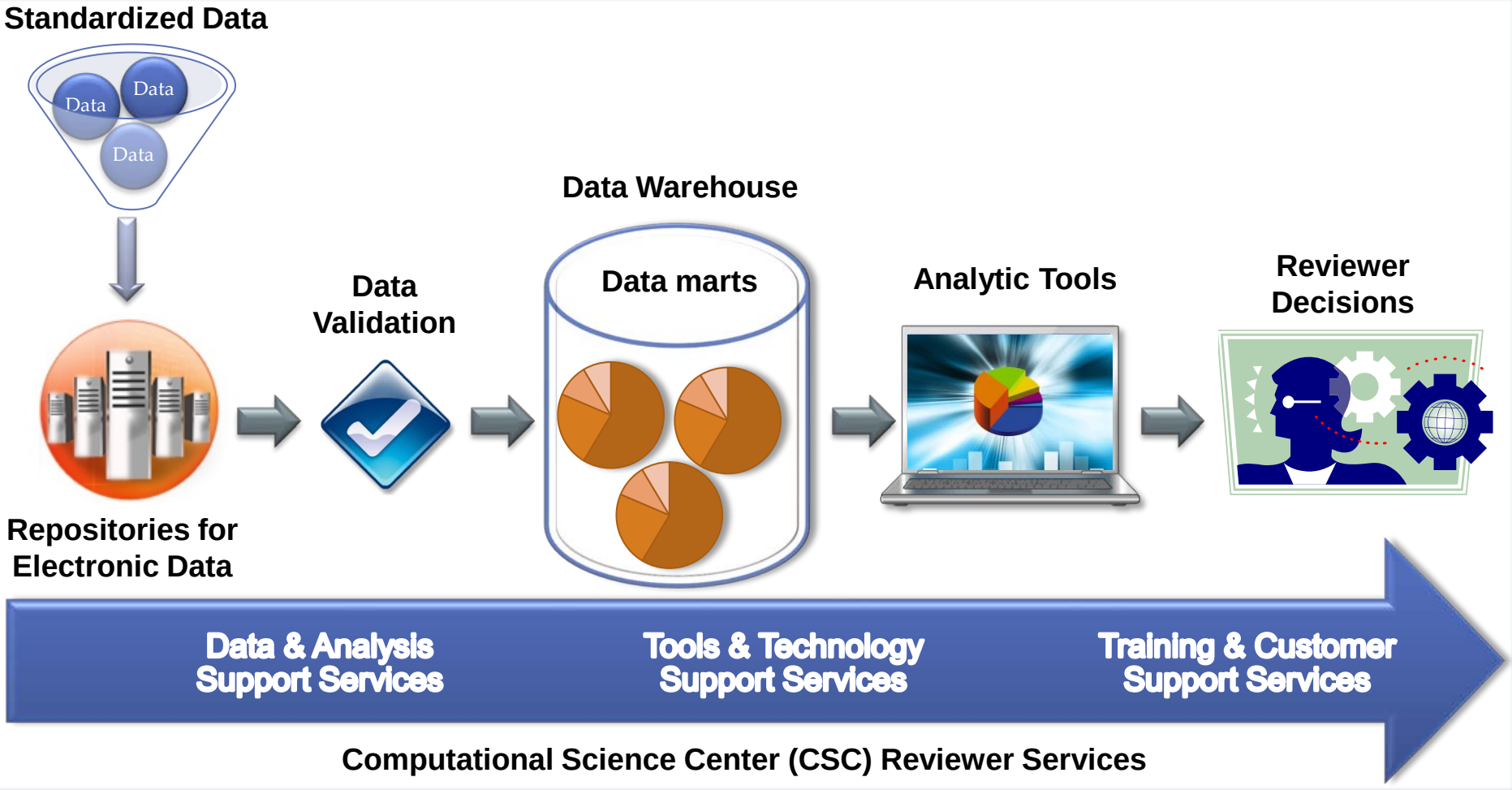
CTR - Big Data Vision

- CTR will evolve into a big data system in the future
- Integrate other data-sets
  - To support the “personalized medicine” paradigm
  - Post marketing data
  - Other Data
- Explore no-SQL and Hadoop in the future

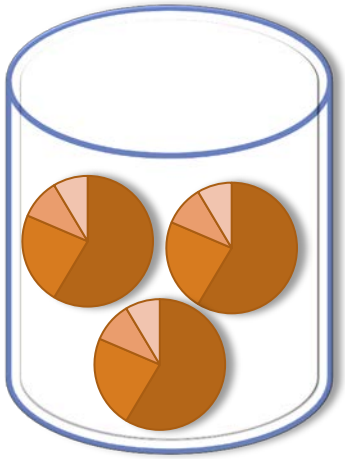
Facilitating Modernization of the Regulatory Review Process



Intersection of data, tools and technology



Data Warehouse and Data Marts



Improve Data Storage/Access

- Develop and implement a clinical trials data warehouse that supports the validation, transformation, loading, and integration of study data
- Support reviewer access to the data via a variety of analytic views (or data marts) and analytic tools

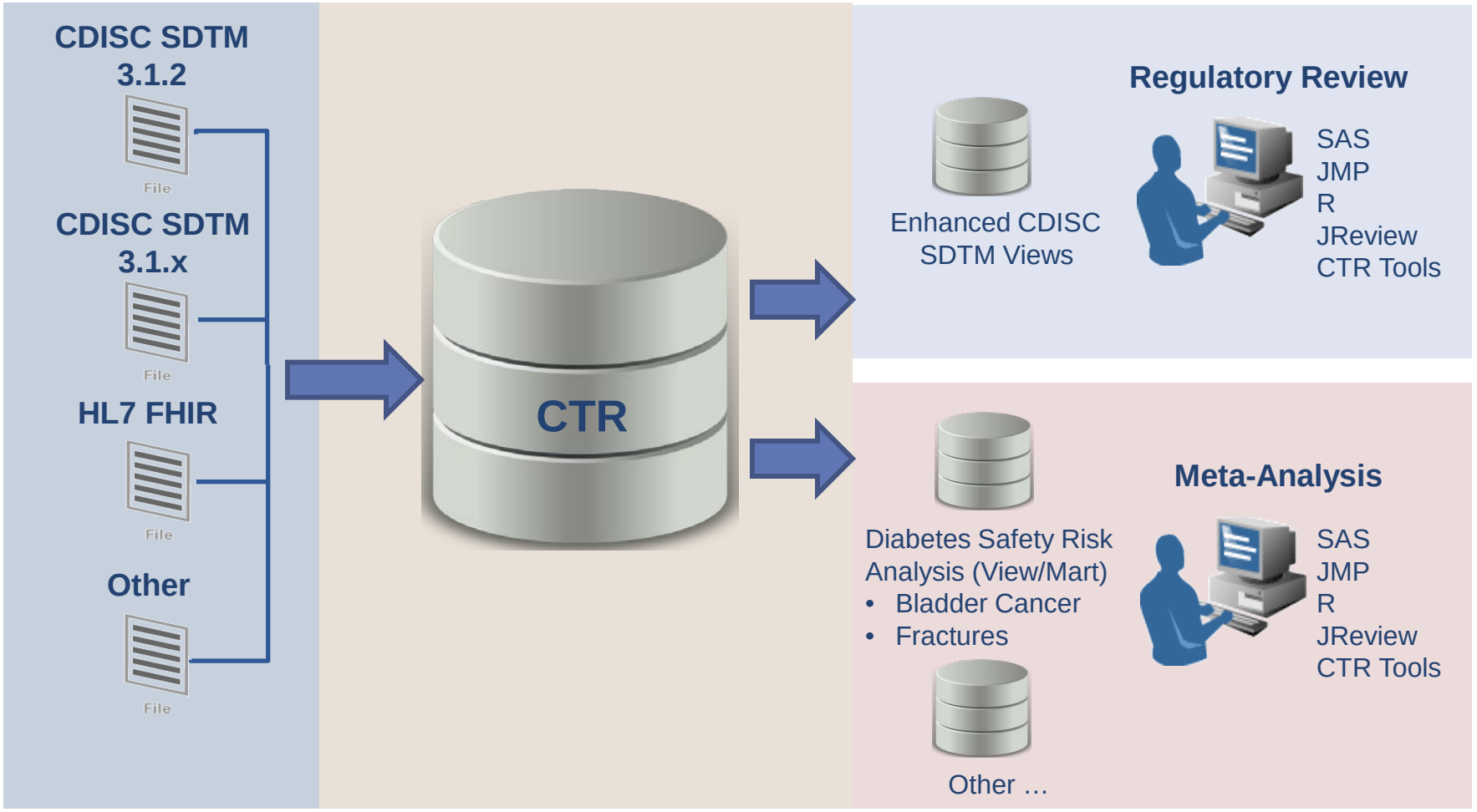
Why Do We Need a Clinical Trials Repository (CTR)?

- Clinical Trials Data will be easily **accessible**
  - One-stop shopping
  - Self-service
- Data will be more **predictable**
  - Consistent in format, content, definitions from study to study, sponsor to sponsor
- Data will be of higher **quality**
  - Data validation service will help insure minimum level of quality data
- Improved productivity
  - Less time needed for routine data management tasks
  - More time to do the analysis & interpret results
- Support Standard Analyses / Reports
- Support Cross-study Analyses

Janus CTR and the 21st Century Drug Review Process

- True potential of standardized data is unleashed with Janus CTR
  - Study data automatically transformed into "views" that are more reviewer-friendly
    - Demographic and Treatment Assignment information in every dataset
    - Numeric Dates
    - Full MedDRA Hierarchy for all adverse events
  - Data "curation" capabilities to
    - Correct misspellings; problems with coding (submitted data is not altered!)
    - Convert lab units to U.S. conventional units
  - Enables pooling of data within an application, across a drug class, or even across drug classes
  - Facilitates timely creation of custom "data marts" to support a variety of meta-analysis needs
- Janus CTR will piloted in early 2014 in to support the JumpStart Service (in parallel with tools currently used)
  - Study Data from applications enrolled in JumpStart will be loaded into CTR

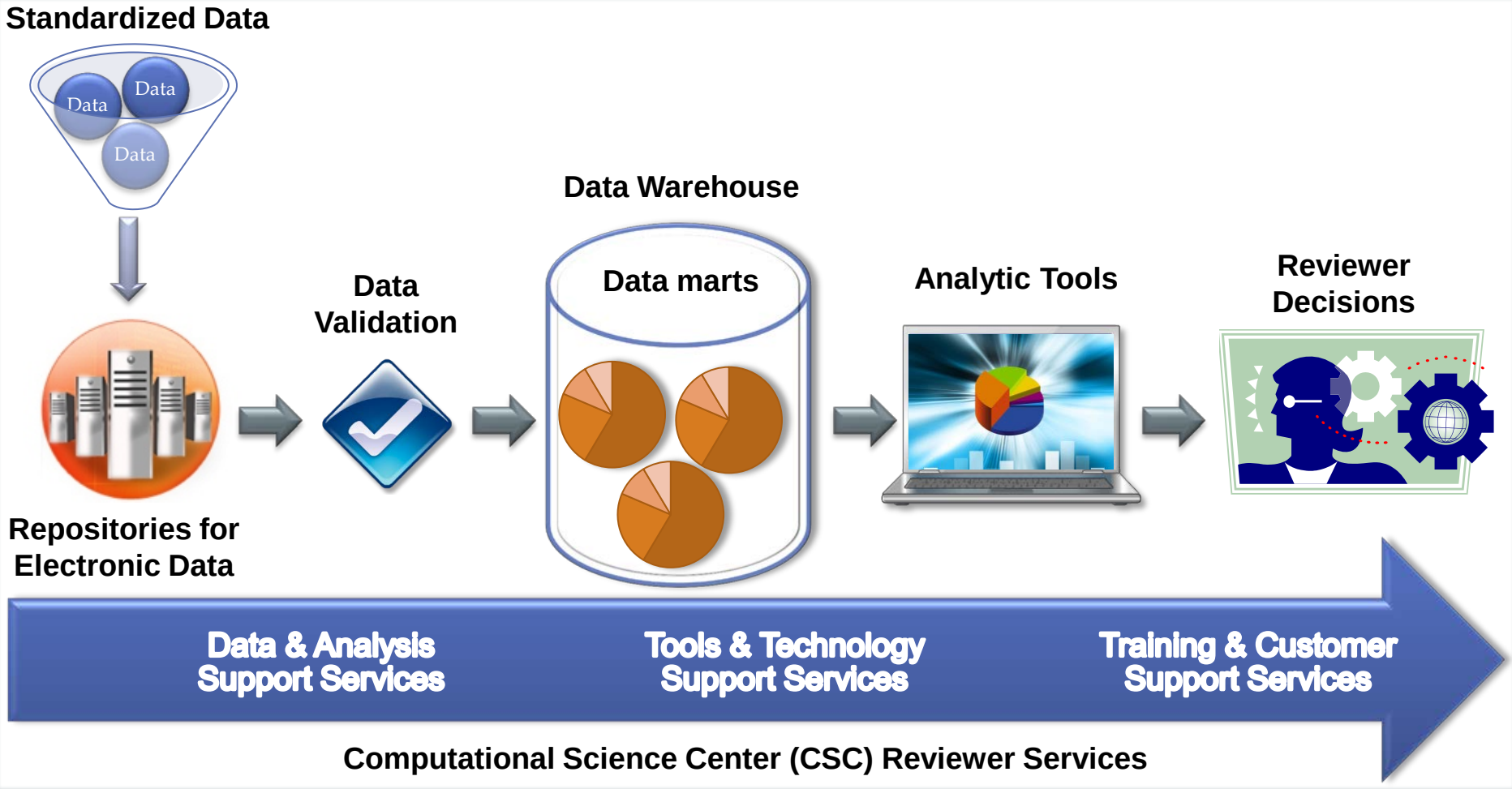
Janus Clinical Trials Repository (CTR)



Janus Clinical Trials Repository

- Supports automated extraction, transformation, loading, management, and reviewer access to standard clinical trials data to support the regulatory review of therapeutic biologic and drug products
- Incorporates data marts designed to address specific needs, such as therapeutic areas, SDTM views for tools, etc.
- Enables queries to be run using various analytic tools from these data marts to meet individual reviewer needs
- Leverages pre-specified analysis scripts and analytic tools

Intersection of data, tools and technology

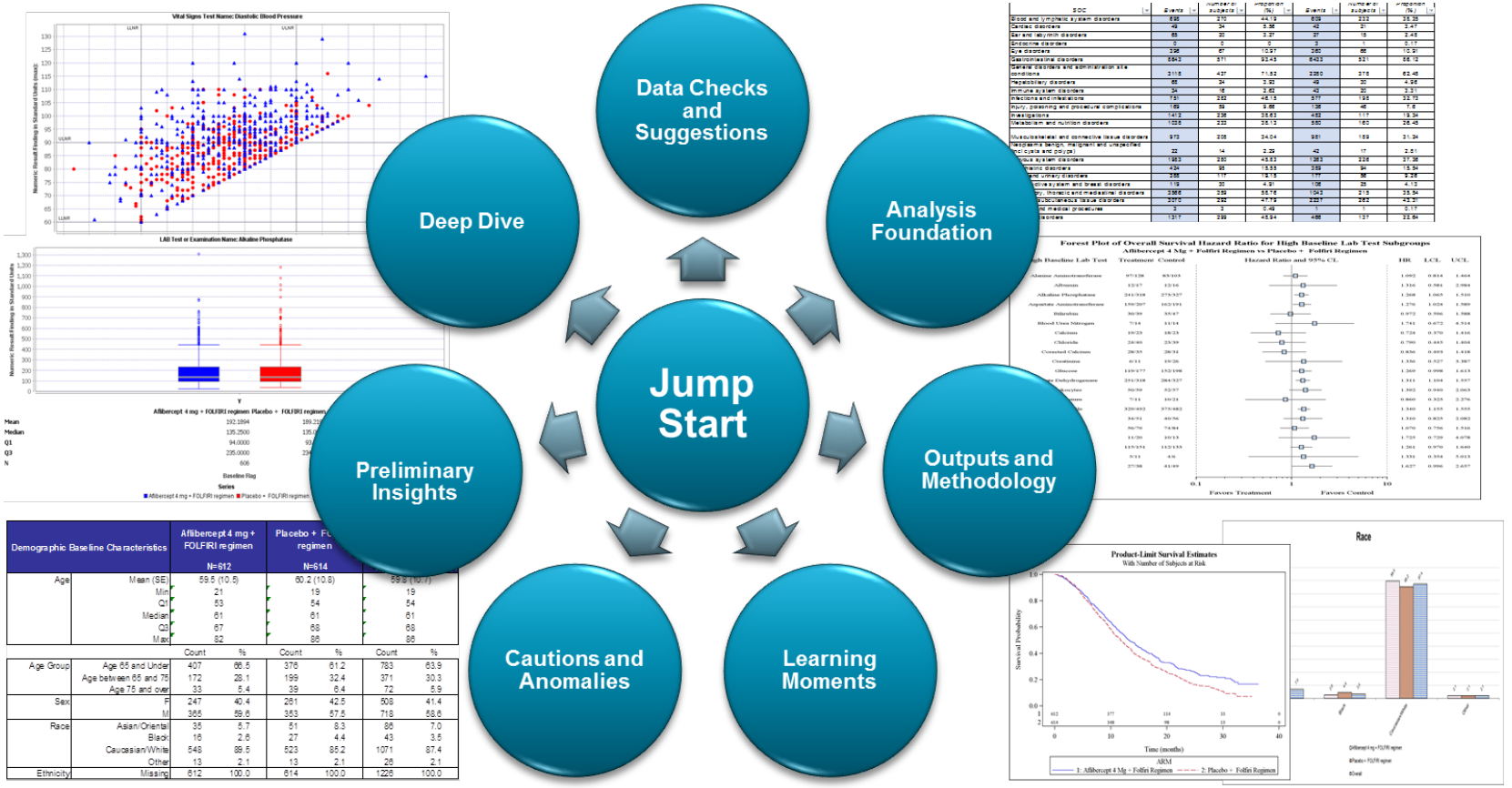


Analytic Tools

Tools	Overview
JReview	• Allows users to tabulate, visualize, and analyze safety and efficacy data • Provides a catalogue of standard analyses with drill down capabilities, making it easy to obtain results and graphical displays of common analyses, such as Hy's Law (relies on availability of SDTM study data)
MAED (MedDRA Adverse Events Diagnostics)	• Allows dynamic and efficient review of adverse event data • Performs over 200 Standardized MedDRA Queries and Adverse Events analyses on all levels of the MedDRA hierarchy in minutes
SAS Analysis Panels	• Provides standard analyses (Demographics, Disposition, Exposure, Adverse Events, and Liver Labs) in Excel or Word
JMP	• Combines powerful statistics with dynamic graphics to enable review process
FDA Investigator's Rapid Review Service (FIRRS)	• Assesses the sponsors' data management and coding quality • Helps reviewers understand the contents of the data
NIMS (Non-clinical Information Management System)	• Enables dynamic study visualization, search, orientation, and analytics capabilities in the review of non-clinical data • Enables cross-study metadata and study data searching across the data repository (across studies, class, findings, and finding types) • Allows reviewers to see all findings for an individual animal in one place

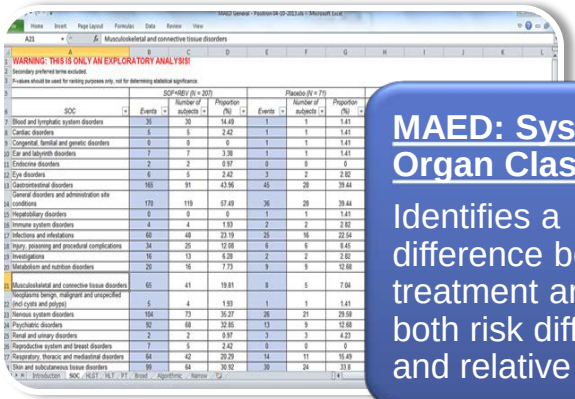
CSC JumpStart Service

Starts a review by performing many standard analyses and identifying key information



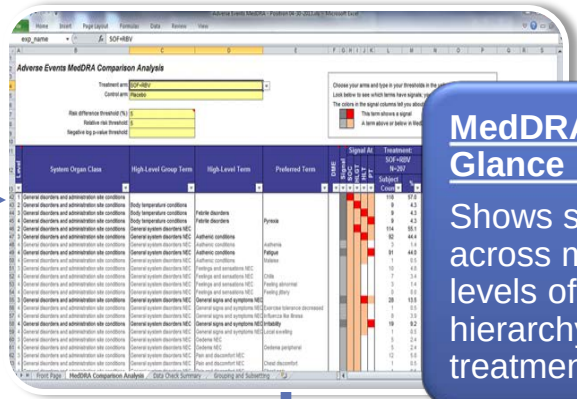
CSC JumpStart Service

- Provides a recommended sequence for using the outputs
- Allows reviewer to follow a safety signal from a high-level to the specific patient details with complementary tools



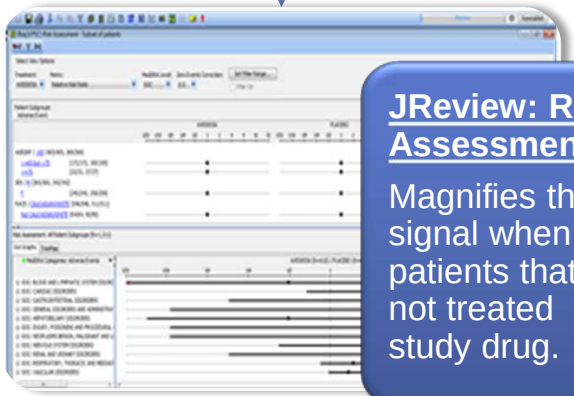
MAED: System Organ Class

Identifies a difference between treatment arms for both risk difference and relative risk.



MedDRA at a Glance Report

Shows same signal across multiple levels of the hierarchy for the treatment arm.



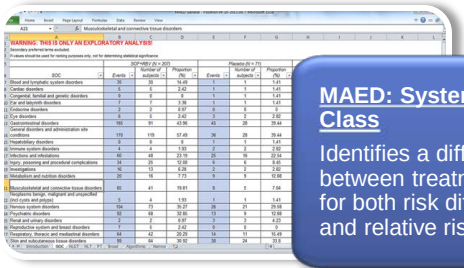
JReview: Risk Assessment

Magnifies the safety signal when viewing patients that were not treated with the study drug.

JReview: Graphical Patient Profile

Shows which patients experienced the Adverse Event shortly after taking a specific concomitant medication.

Planned CTR Support of JumpStart Service



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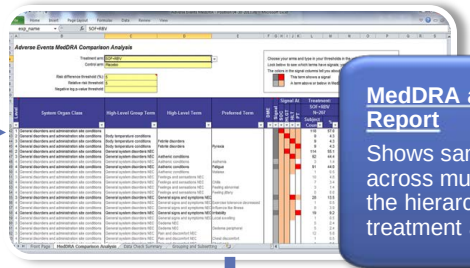

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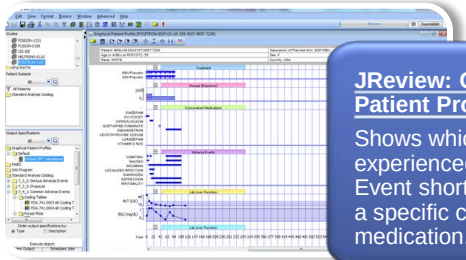

JReview: Graphical Patient Profile

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Enhanced CDISC SDTM Views

Additional Views to Support Regulatory Review

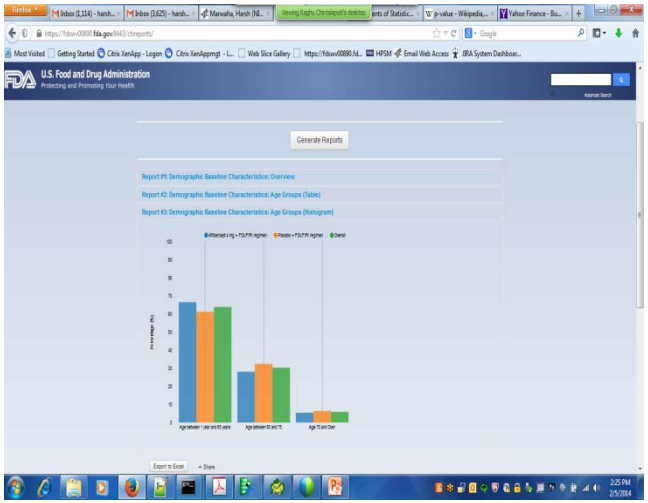
Regulatory Review

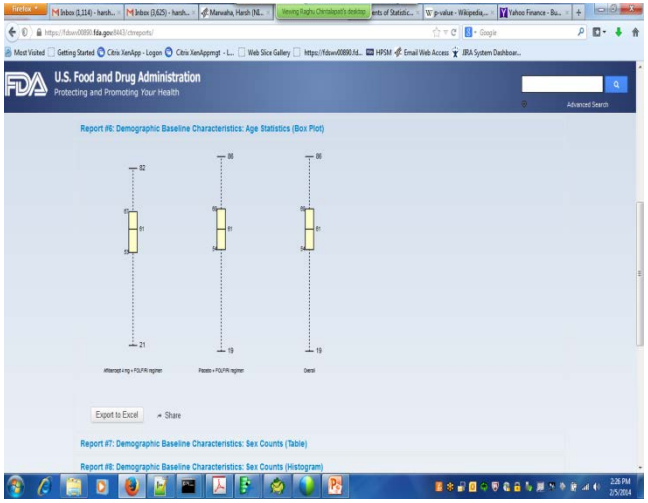
SAS
JMP
R
JReview
CTR Tools

CTR Tools to Support JumpStart

- CTR Standard Analysis Reports (web-based application)
  - Standardized reports that support safety review, including safety reports supported by JumpStart
- Study & Standards Browser (web-based application)
- Ad Hoc Query Tool (web-based application)
- Data Curation

CTR Reports





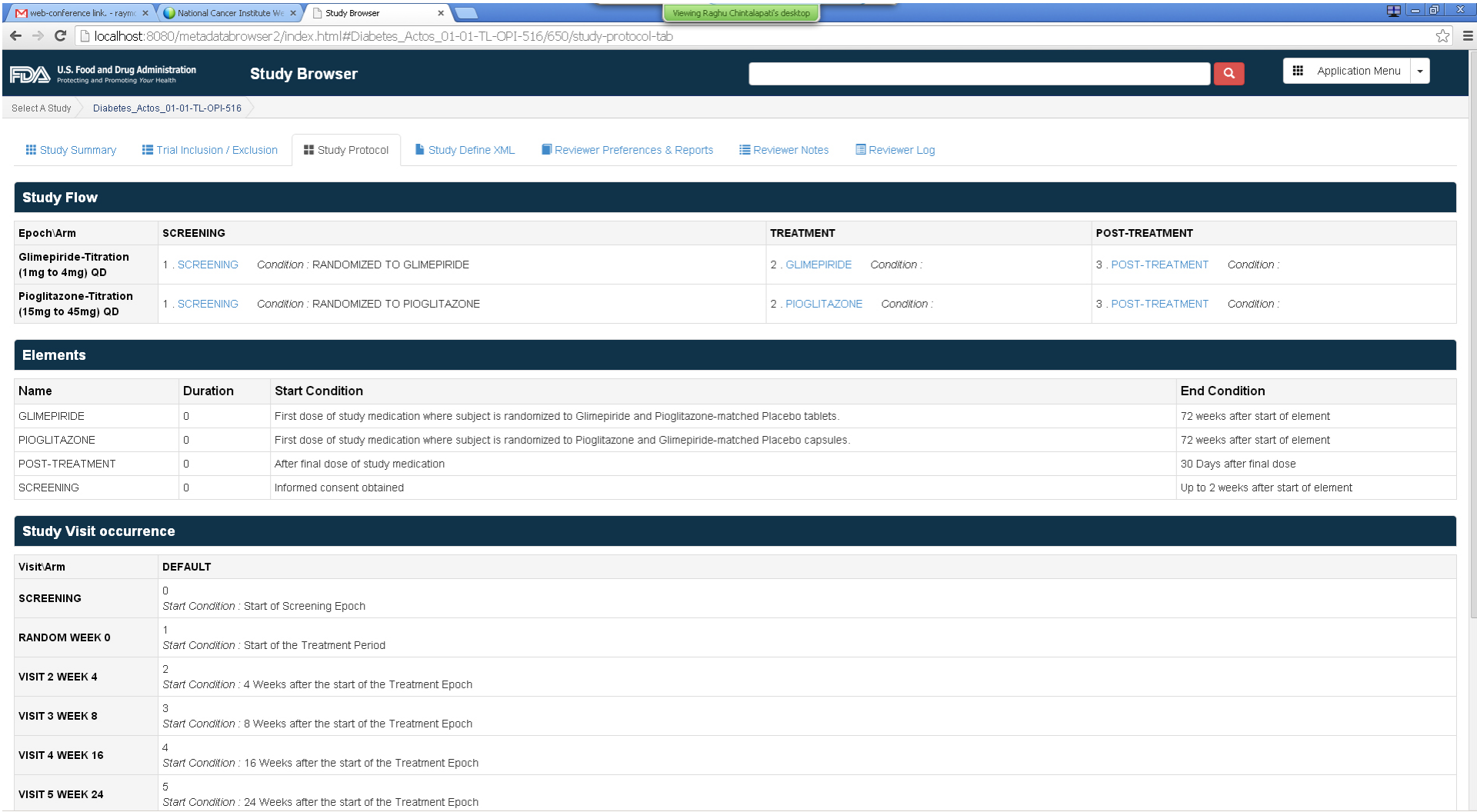
- Over 60 standardized reports
- Includes MAED, FIRRS and standard analysis reports.
- Users can filter data prior to running each report

Study & Standards Browser

- Consolidates all study meta-data
  - Access summary information about the study (Study design, trial summary, explanation of codes used, location of specific variables, etc.)
  - Study specific transforms, preferences and reports
  - User defined tags for other meta-data

- Reviewer Log
  - Ability to go back in time and recreate analyses

Study & Standards Browser



Study Flow

Epoch\Arm	SCREENING	TREATMENT	POST-TREATMENT
Glimepiride-Titration (1mg to 4mg) QD	1 . SCREENING *Condition :* RANDOMIZED TO GLIMEPIRIDE	2 . GLIMEPIRIDE *Condition :*	3 . POST-TREATMENT *Condition :*
Pioglitazone-Titration (15mg to 45mg) QD	1 . SCREENING *Condition :* RANDOMIZED TO PIOGLITAZONE	2 . PIOGLITAZONE *Condition :*	3 . POST-TREATMENT *Condition :*

Elements

Name	Duration	Start Condition	End Condition
GLIMEPIRIDE	0	First dose of study medication where subject is randomized to Glimepiride and Pioglitazone-matched Placebo tablets.	72 weeks after start of element
PIOGLITAZONE	0	First dose of study medication where subject is randomized to Pioglitazone and Glimepiride-matched Placebo capsules.	72 weeks after start of element
POST-TREATMENT	0	After final dose of study medication	30 Days after final dose
SCREENING	0	Informed consent obtained	Up to 2 weeks after start of element

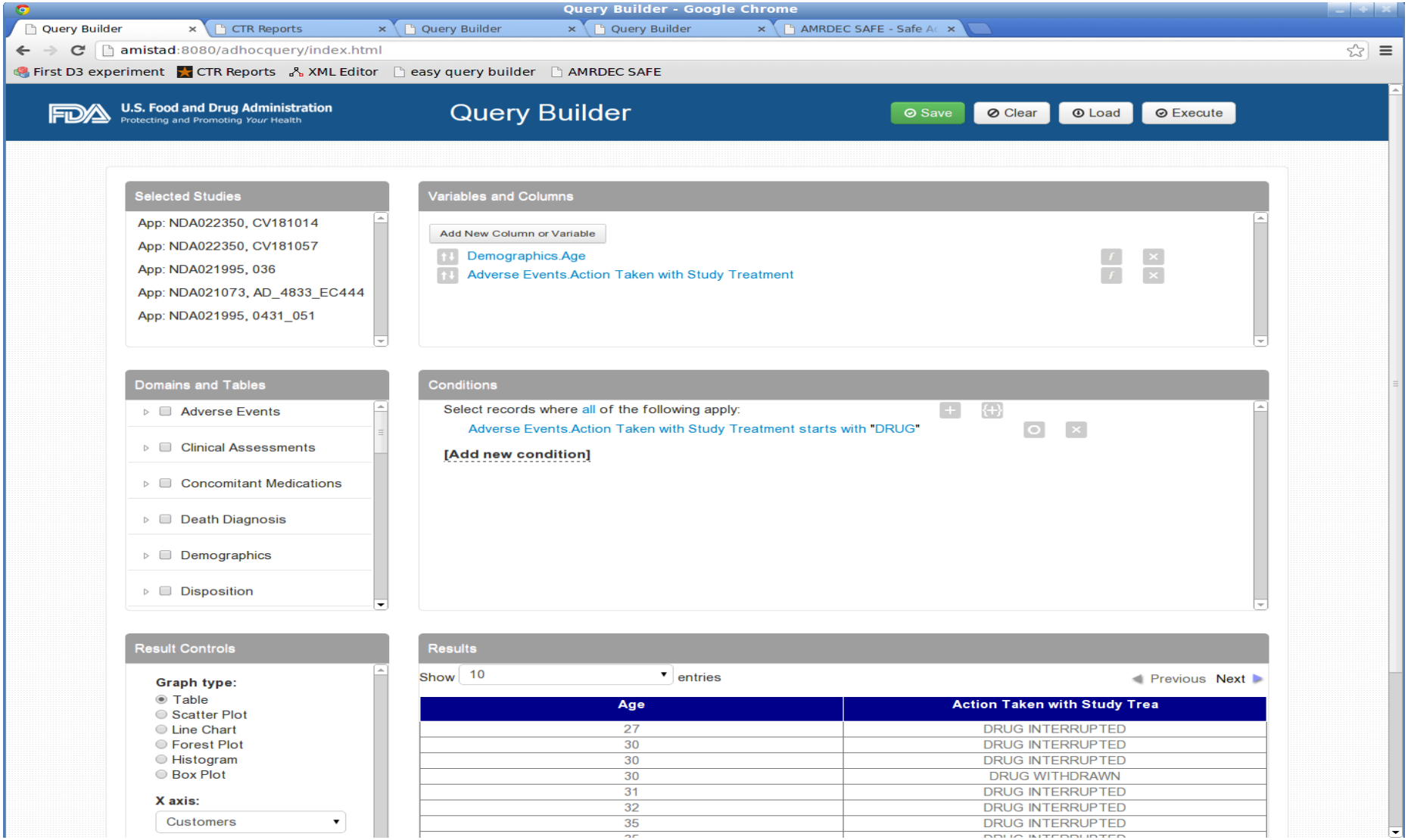
Study Visit occurrence

Visit\Arm	DEFAULT
SCREENING	0 *Start Condition :* Start of Screening Epoch
RANDOM WEEK 0	1 *Start Condition :* Start of the Treatment Period
VISIT 2 WEEK 4	2 *Start Condition :* 4 Weeks after the start of the Treatment Epoch
VISIT 3 WEEK 8	3 *Start Condition :* 8 Weeks after the start of the Treatment Epoch
VISIT 4 WEEK 16	4 *Start Condition :* 16 Weeks after the start of the Treatment Epoch
VISIT 5 WEEK 24	5 *Start Condition :* 24 Weeks after the start of the Treatment Epoch

Ad-Hoc Query Tool

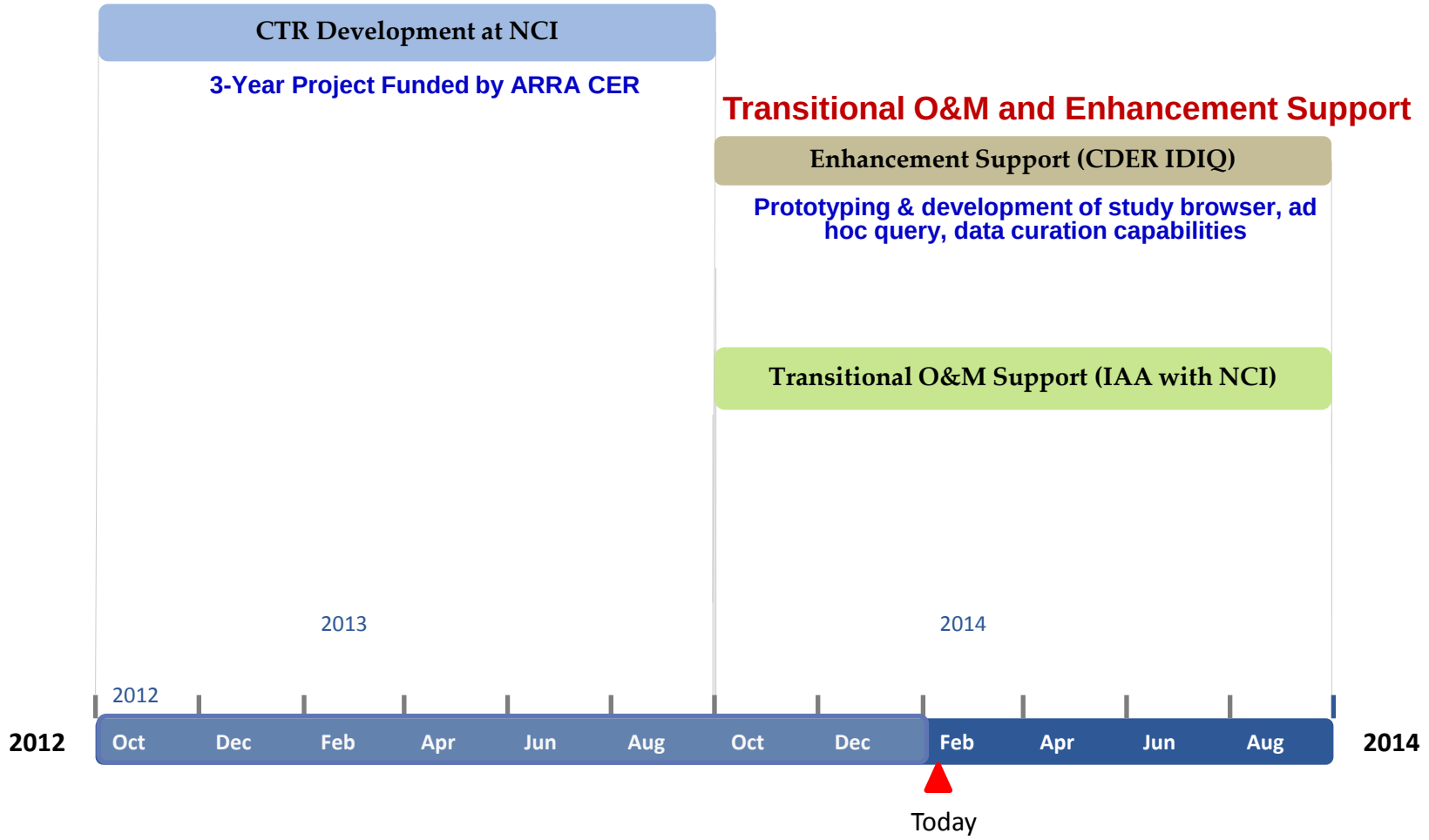
- Allows reviewers to manipulate data by
  - Pooling of data across studies
  - Filtering
  - Sub-setting
  - Complex queries with logical operators
- Reviewers can create and download customized analysis ready datasets from the CTR
  - From a single study
  - Across multiple studies
- Provides a framework for developing meta-analysis reports

Ad-Hoc Query Tool



Timeline for Janus Clinical Trials Repository 2012 through 2014

Contractor Support through NCI/SAIC-Frederick



Future Directions

- CTR marks the first step to integration of diverse and bigger data
  - CTR is designed to handle large data-sets
  - Is expected to grow into a very large data warehouse with many data marts.
  - Expected to grow by a few TB's every year
- CTR will evolve into a big data system in the future
- Integrate other data-sets
  - To support the "personalized medicine" paradigm
  - Pre market and Post marketing data
  - Other Data (pharmacogenomics, large simple trials, therapeutic area specific databases
  - Support nonclinical data to clinical correlations

Conclusion

- Rapidly moving towards a modernized, integrated bioinformatics-based review environment
- High quality, standardized data
- Easy data analysis using leading practices
- Access to powerful, standard data-based review tools