The Review of SDTM Datasets at CDER: A Clinical Reviewer's Perspective

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Overview

- Before SDTM
- After SDTM

CDER Now Accepts SDTM Datasets

FOR IMMEDIATE RELEASE
P04-73
July 21, 2004

FDA Announces Standard Format That Drug Sponsors Can Use to Submit Human Drug Clinical Trial Data

(http://www.fda.gov/bbs/topics/news/2004/NEW01095.html)

"The importance of a standard for the exchange of clinical trial data cannot be overstated. FDA reviewers spend far too much valuable time simply reorganizing large amounts of data submitted in varying formats. Having the data presented in a standard structure will improve FDA's ability to evaluate the data and help speed new discoveries to the public."

-Lester Crawford, Acting Commissioner, FDA

Before SDTM

- Domains = Yes
- Standard Domain Names = No
- Standard Structure = No
- Standard Variables = No
- Standard Variable Names = No
- Standard Terms = No

Before SDTM

Result:

- Steep “Learning Curve” for each application / Study
- Reviewers had to familiarize themselves with unique data structure, domain names, variables and variable names used in an application
- TIME CONSUMING

Before SDTM

- Sometimes: different variable names/terms within the same application (!)
- e.g. same lab test, two names:
  SGOT = AST
- Pooling, joining datasets awkward, difficult
- Good portion of review time spent "cleaning up the data"
- Inefficient, error-prone

After SDTM

- Domains = Yes
- Standard Domain Names = Yes
- Standard Structure = Yes
- Standard Variables = Yes
- Standard Variable Names = Yes
- Standard Terms = not yet, but coming

After SDTM

- Standard Domain Names = Easy to Find Data
- Standard Structure = Easy to Understand the Data
- Standard Variables/Variable Names = Immediate Familiarity with the Data
- Consistency
- Minimal learning curve
- TIME EFFICIENT

Benefits of SDTM

- Development of standardized review strategies and tools to store, display, analyze the data
- COTS Tools: e.g. JMP
- Custom Tools:
  - JANUS
  - WebSDM
  - PPV

JMP

- COTS software
- FDA site license; available to all reviewers
- Data exploration and analysis
- Familiar to Reviewers
- Available now

JMP and SDTM

SDTM presents unique challenges:

- Demographic/Treatment Assignment info not in all domains
- Character date fields
- One row per observation – how to do change from baseline calculations?

Using JMP to Analyze SDTM datasets

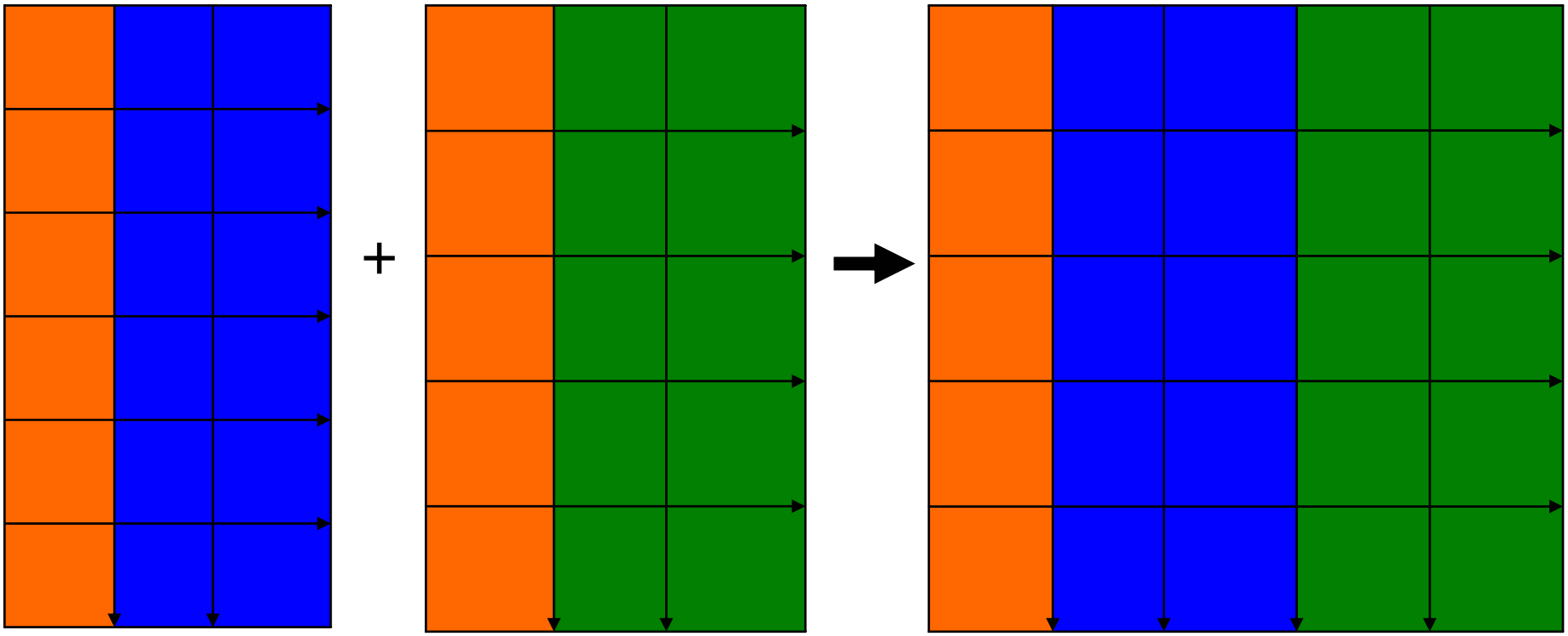
- Reviewer Re-education and Re-Training
- New internal JMP training manual
- Revamp internal JMP training curriculum

Join Command

- Allows addition of key demographic and treatment assignment variables to any domain
- Standard allows creation of JMP script to automate task
- JOIN DM script command being incorporated into standard JMP install

JOIN Command

DM AE

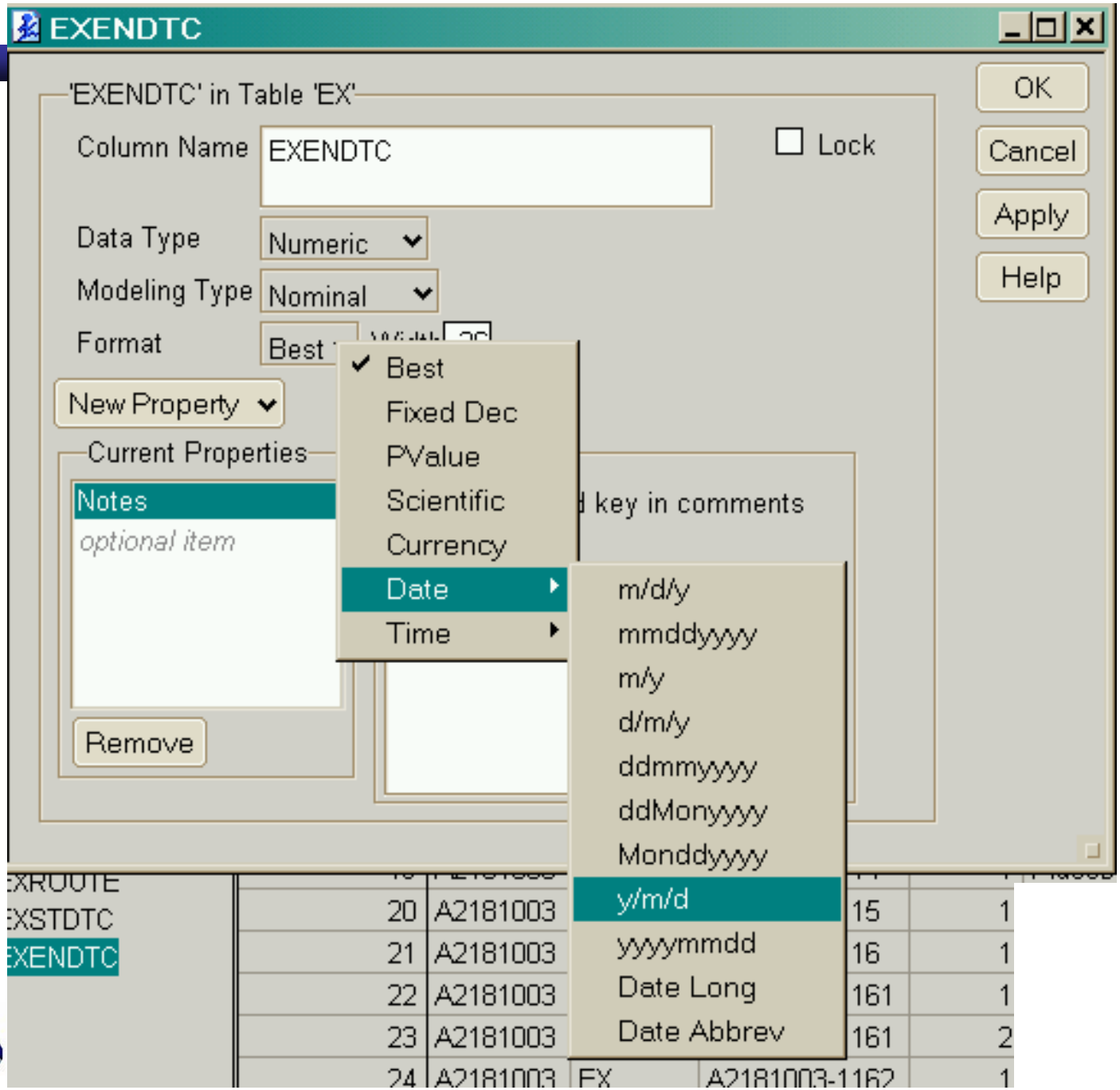


SDTM Dates and JMP

- ISO 8601 Standard
- Character Fields

1997-07-16T19:20:30

- Must convert to numeric fields to perform date calculations, e.g. duration of exposure
- JMP Version 5.1.1 supports ISO 8601 standard
- We are upgrading all users to V. 5.1.1


EXENDTC
'EXENDTC' in Table 'EX'
Column Name
EXENDTC
Lock
Data Type
Numeric
Modeling Type
Nominal
Format
Best
OK
Cancel
Apply
Help
New Property
Current Properties
Notes
optional item
Remove
key in comments
Best
Fixed Dec
PValue
Scientific
Currency
Date
Time
m/d/y
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ddmmyyyy
ddMonyyyy
Monddyyyy
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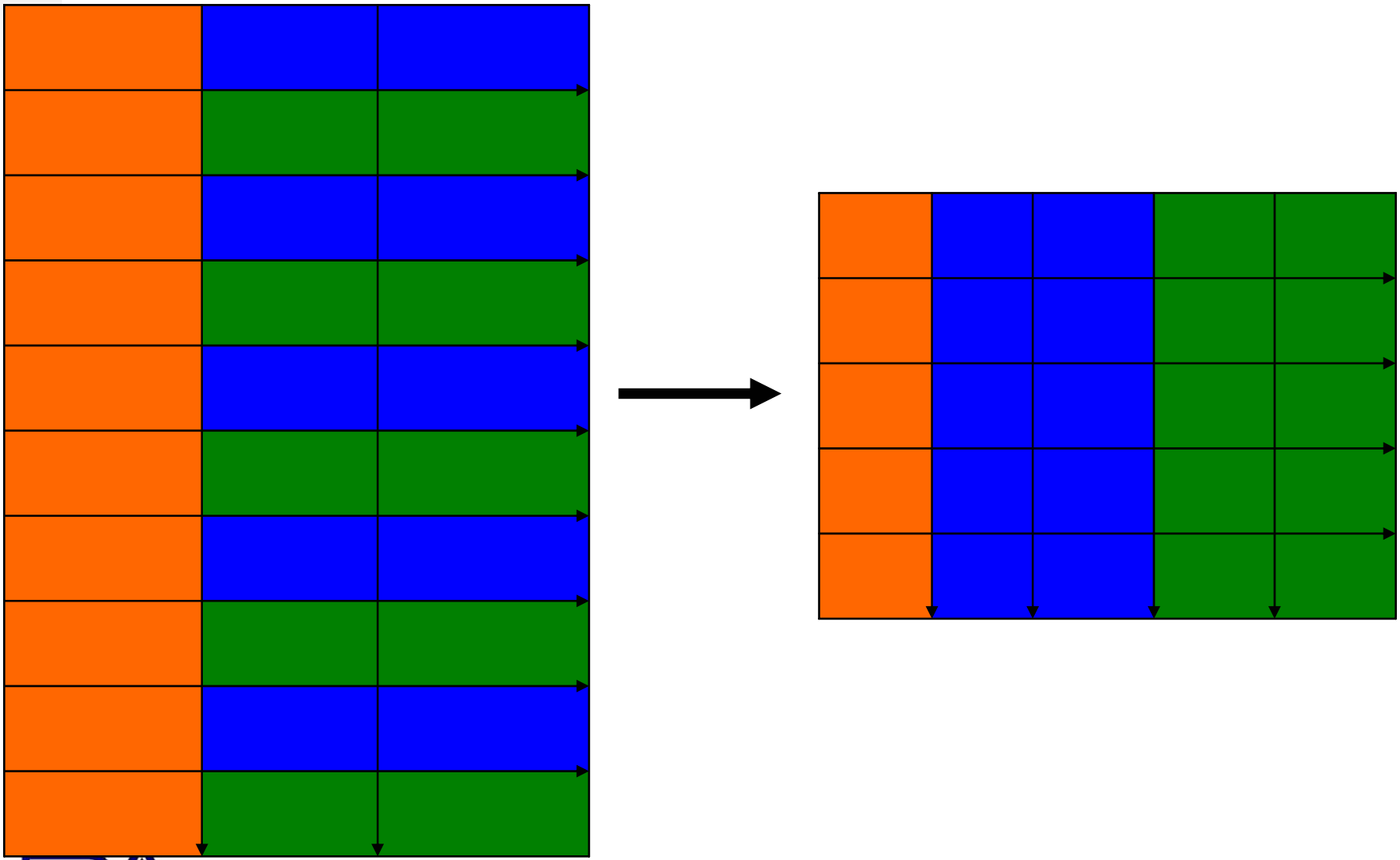
Date Long
Date Abbrev
XROUTE
XSTDTC
XENDTC
20 A2181003
21 A2181003
22 A2181003
23 A2181003
24 A2181003 EX A2181003-1162
15 1
16 1
161 1
161 2
1

Change from Baseline Analyses

- Tall – Skinny (vertical) Organization
- Baseline measurements in a separate row

- Use SPLIT command to bring baseline measurements on same row (horizontal structure)
- Makes change from baseline analyses easy!

SPLIT Command



Conclusion: JMP and SDTM

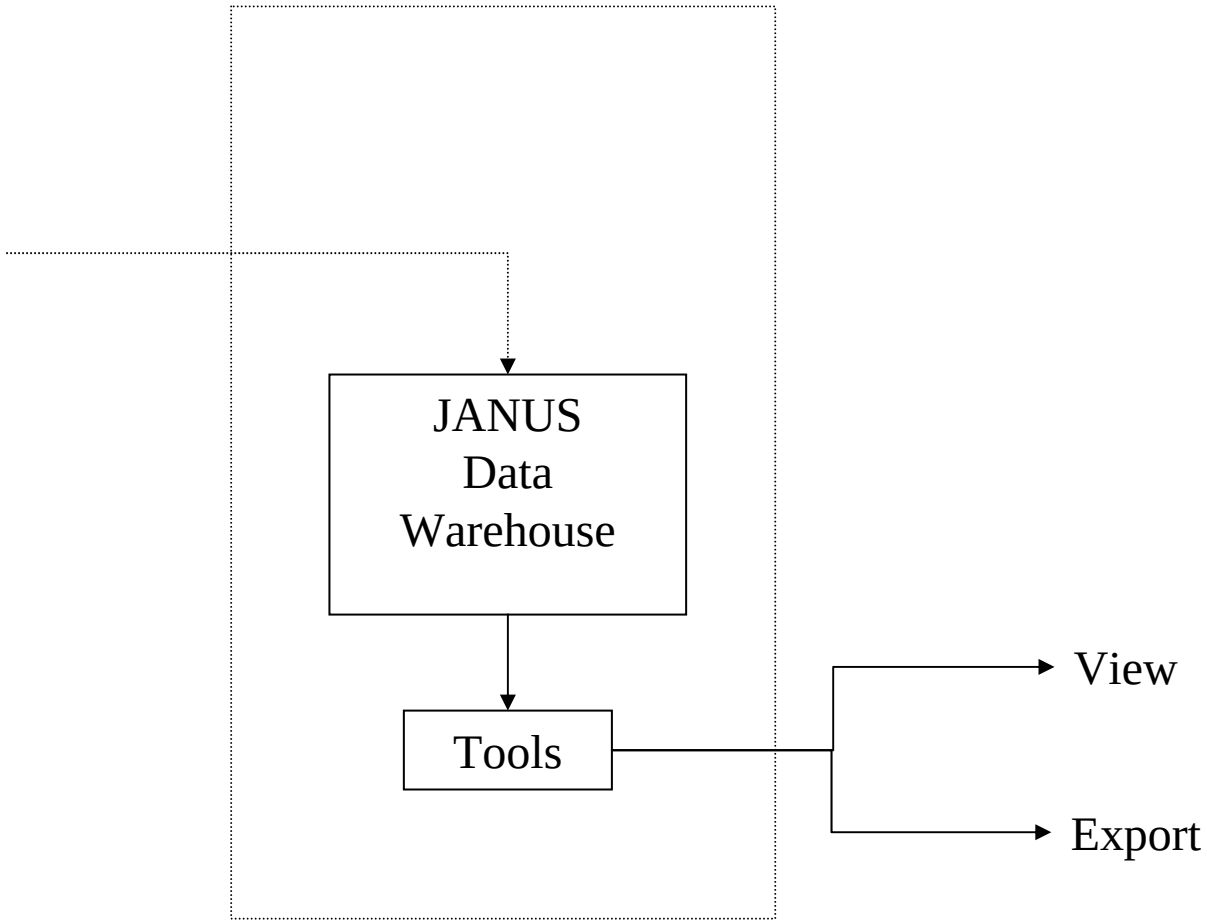
- JMP continues to be a powerful, flexible tool to explore and analyze data in all formats, including SDTM
- Available NOW
- New techniques/training necessary to handle SDTM data
- Standard data format allow development of JMP scripts to automate frequently performed steps

JANUS

- Data Warehouse / Repository
- Facilitates Cross-Application analyses (e.g. investigation of adverse events in an entire therapeutic class)

JANUS and Study Data Environment

Standard
- Observations
- Metadata
- Protocol
- Audit trail



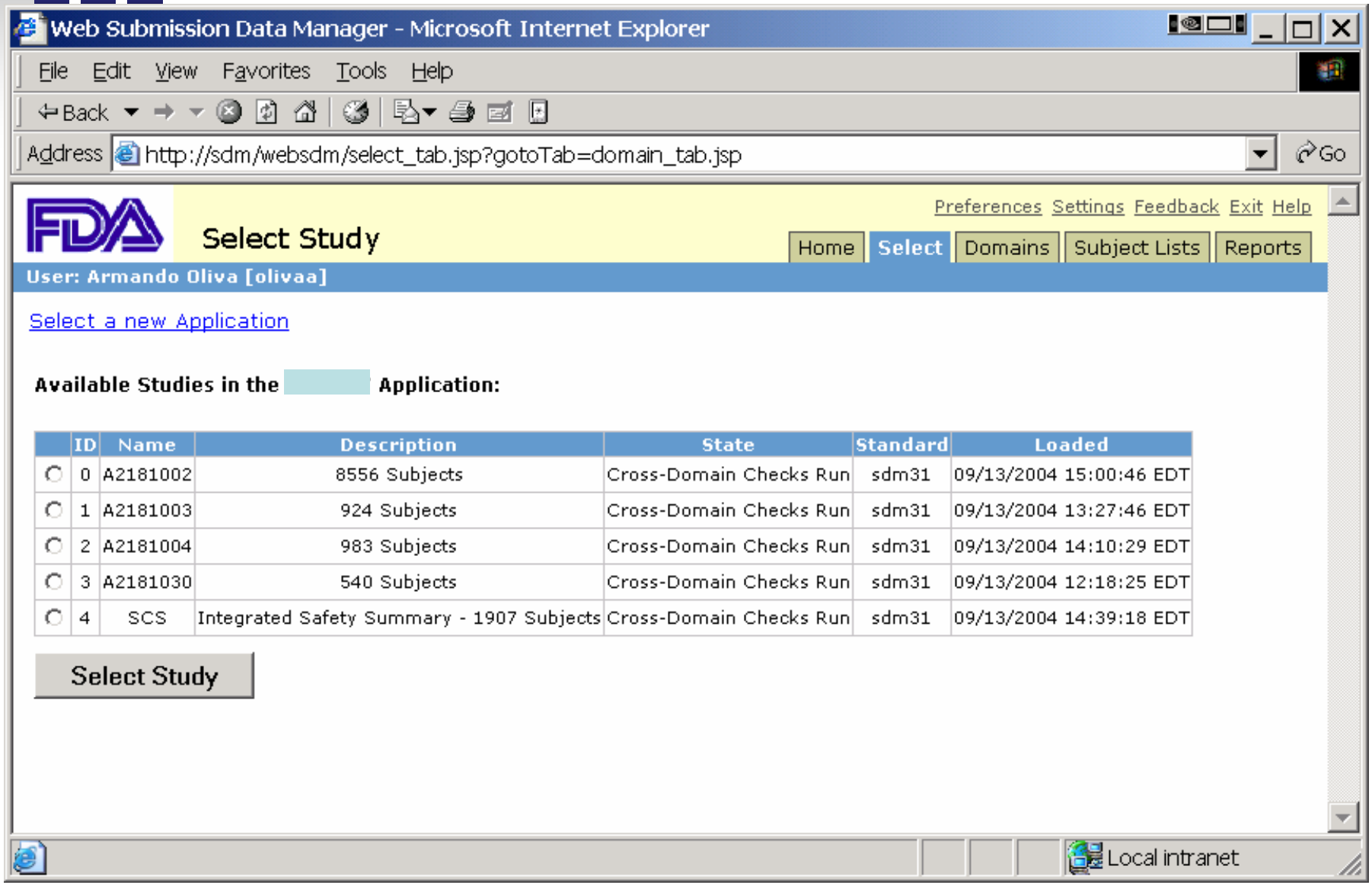
Submission **Repository** **Review**

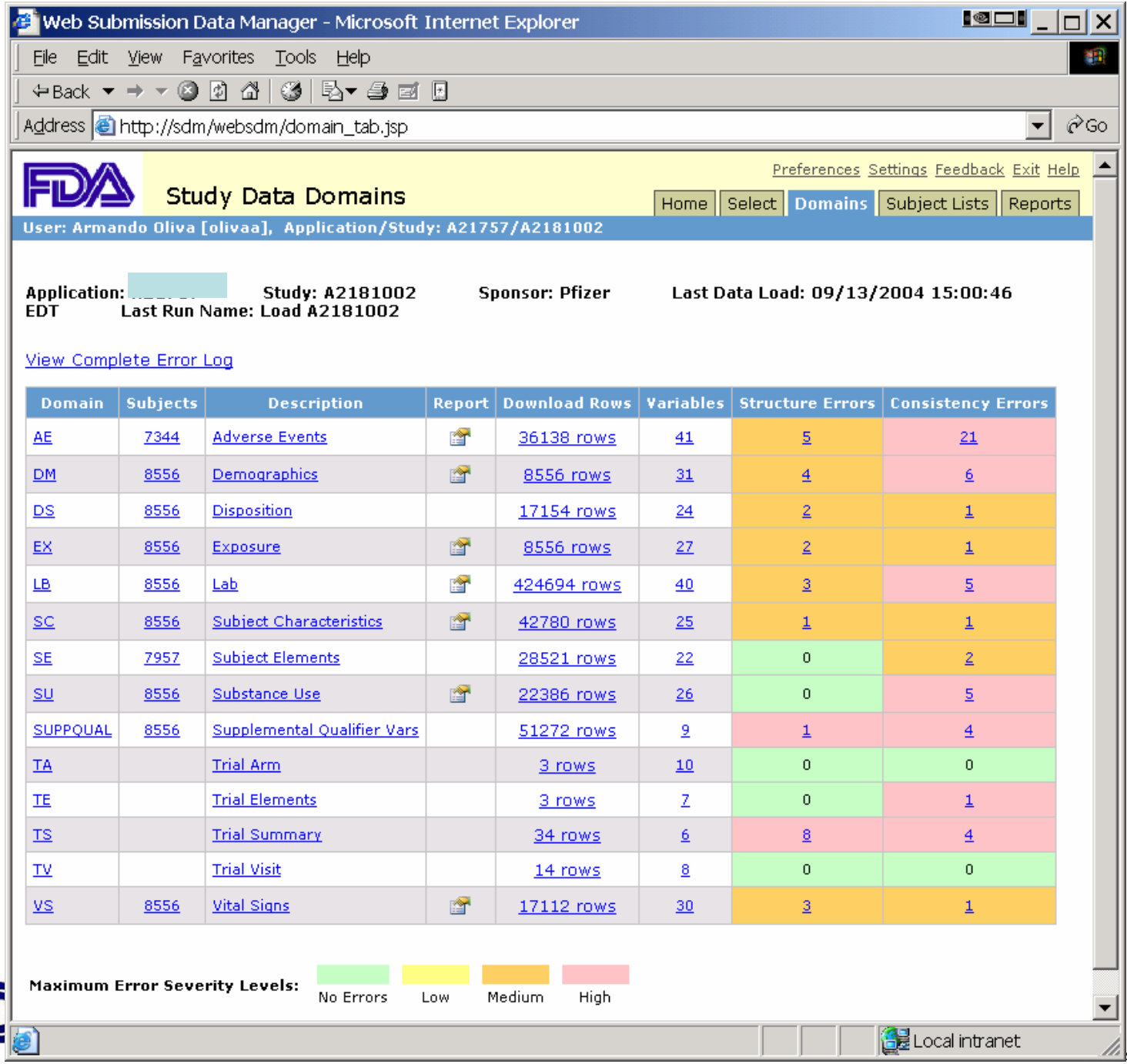
WebSDM

- ***Web***-based ***S***ubmission ***D***ata ***M***anager
- Provides Access, Displays of the Data
- Validates incoming files for conformance with SDTM
- Provides standard analyses of the data (customizable)
- Export data to various file types (.csv, .xpt, .sas, .xls)

WebSDM (cont'd)

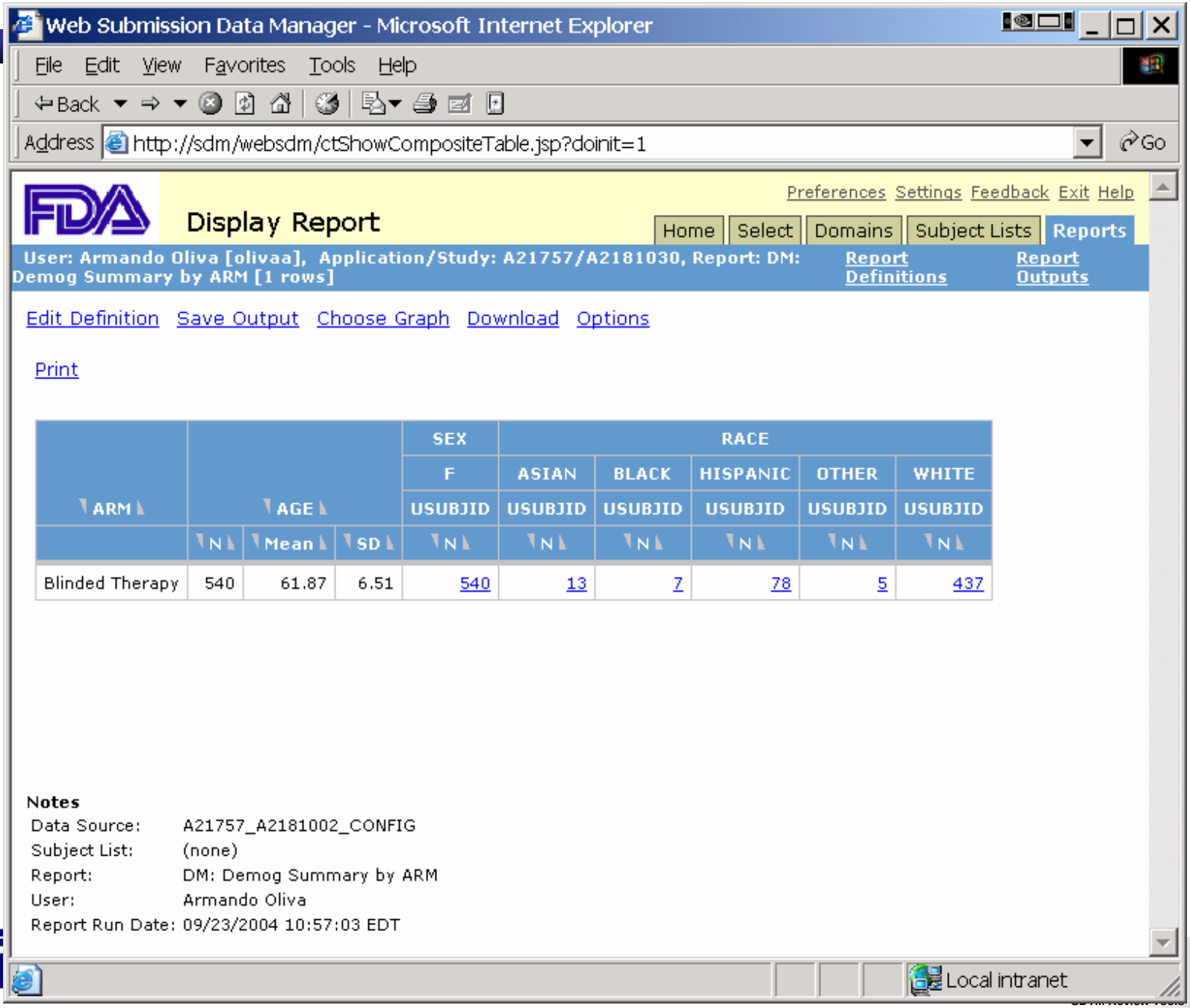
- Provides audit trail of transformation/reports made by Reviewers
- Automatically joins data with other domains (DM, SUPPQUAL)
- Flips data for Findings into horizontal views (e.g., by visit or by test); easier to review


Web Submission Data Manager - Microsoft Internet Explorer
File Edit View Favorites Tools Help
Back
Address http://sdm/websdm/select_tab.jsp?gotoTab=domain_tab.jsp
Go
Select Study
Preferences Settings Feedback Exit Help
Home Select Domains Subject Lists Reports
User: Armando Oliva [olivaa]
Select a new Application
Available Studies in the Application:
ID Name Description State Standard Loaded
0 A2181002 8556 Subjects Cross-Domain Checks Run sdm31 09/13/2004 15:00:46 EDT
1 A2181003 924 Subjects Cross-Domain Checks Run sdm31 09/13/2004 13:27:46 EDT
2 A2181004 983 Subjects Cross-Domain Checks Run sdm31 09/13/2004 14:10:29 EDT
3 A2181030 540 Subjects Cross-Domain Checks Run sdm31 09/13/2004 12:18:25 EDT
4 SCS Integrated Safety Summary - 1907 Subjects Cross-Domain Checks Run sdm31 09/13/2004 14:39:18 EDT
Select Study
Local intranet



Domain	Subjects	Description	Report	Download Rows	Variables	Structure Errors	Consistency Errors
AE	7344	Adverse Events		36138 rows	41	5	21
DM	8556	Demographics		8556 rows	31	4	6
DS	8556	Disposition		17154 rows	24	2	1
EX	8556	Exposure		8556 rows	27	2	1
LB	8556	Lab		424694 rows	40	3	5
SC	8556	Subject Characteristics		42780 rows	25	1	1
SE	7957	Subject Elements		28521 rows	22	0	2
SU	8556	Substance Use		22386 rows	26	0	5
SUPPQUAL	8556	Supplemental Qualifier Vars		51272 rows	9	1	4
TA		Trial Arm		3 rows	10	0	0
TE		Trial Elements		3 rows	7	0	1
TS		Trial Summary		34 rows	6	8	4
TV		Trial Visit		14 rows	8	0	0
VS	8556	Vital Signs		17112 rows	30	3	1

Maximum Error Severity Levels: No Errors Low Medium High

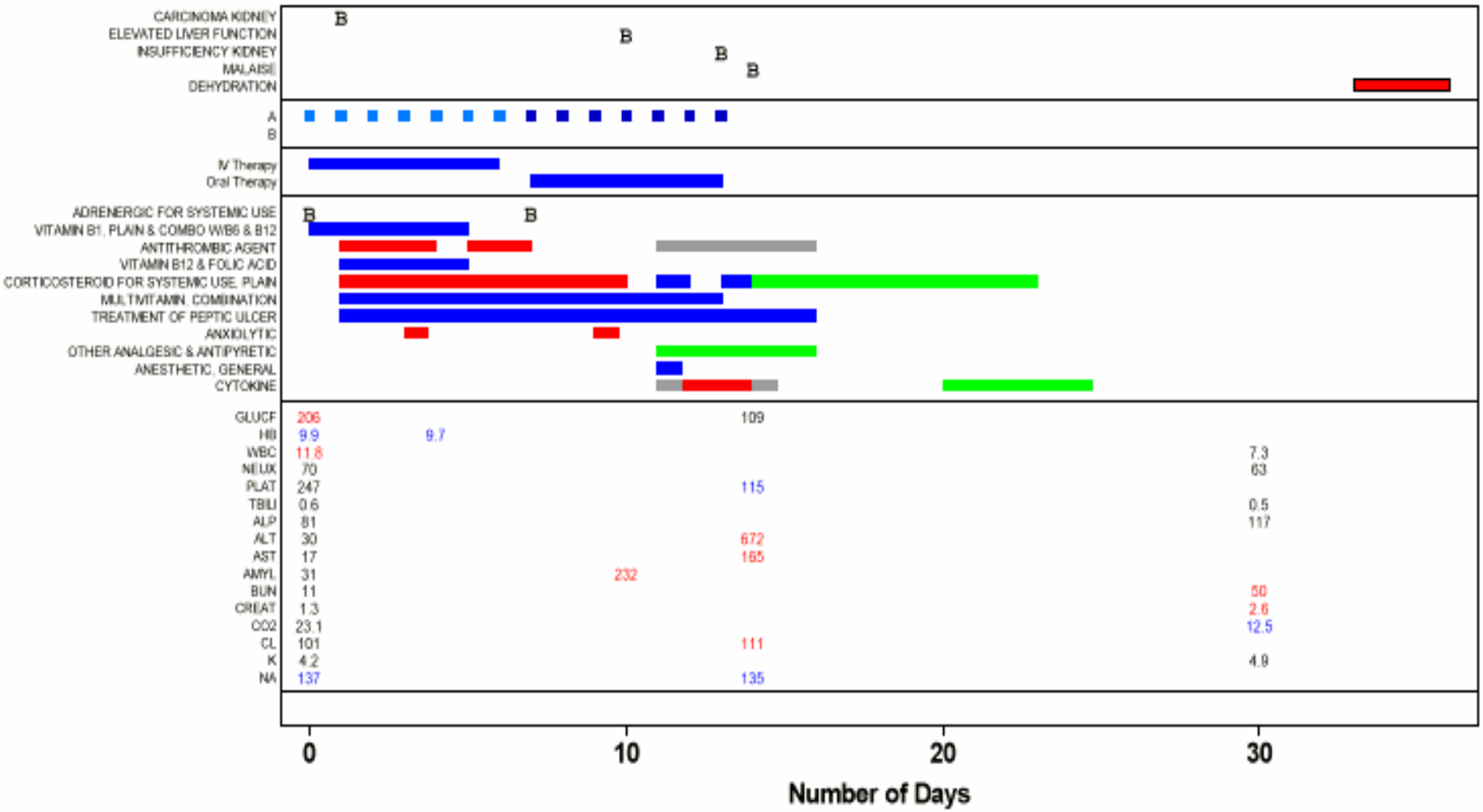


ARM	AGE			SEX	RACE				
				F	ASIAN	BLACK	HISPANIC	OTHER	WHITE
				USUBJID	USUBJID	USUBJID	USUBJID	USUBJID	USUBJID
	N	Mean	SD	N	N	N	N	N	N
Blinded Therapy	540	61.87	6.51	540	13	7	78	5	437

Patient Profile Viewer (PPV)

- Allows graphical display of clinical trial data for a single patient

Patient Profile



Summary

- Ongoing training and education allows users to use JMP to analyze SDTM datasets
- Development of custom scripts and review tools is also ongoing
- Increases in reviewer efficiency