Visualising CDISC SDTM for Monitoring and Review

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Visualising CDISC SDTM for Monitoring and Review

1. Bringing CDISC SDTM Alive with Spotfire and SAS
2. Resolving an Industry Challenge
3. The Power of Standardisation
4. CDISC SDTM Based Visualizations
5. CFAST Therapeutic Area Support
6. CDISC SDTM Challenges Encountered
7. Questions
Bringing CDISC SDTM Alive with Spotfire and SAS
How to deliver cost effective, timely and practical (e.g. intuitive, interactive and comprehensive) data review systems for any given clinical trial regardless of therapeutic area

This can be achieved through leveraging an existing and established industry standard (CDISC SDTM), TIBCO Spotfire and SAS

Our Preclarus® Patient Data Dashboard (PDD) is delivering results, for example:

- Identified an increase in infections which contributed to discussions towards a protocol amendment
- Subjects efficiently reviewed during dose escalation review meetings
- A reduction in study specific Patient Profile requests for medical review
The Power of Standardization

+ Through CDISC SDTM standards, comprehensive data review systems can be designed for any future clinical trial
  + **Scalable**: The same platform is deployed on any study that has CDISC SDTM data
  + **Comprehensive and Intuitive**: reproducibility means centralized and specialist investment that gets the system right
  + **Cost effective**: There is no requirement for study specific customization, so it’s effectively free where SDTM is available. Reduction in safety review listings
  + **Quick to deploy**: The Preclarus PDD engine is built using TIBCO Spotfire, SAS and SDTM standards in advance, not designed off study data. Simply upload new SDTM data into the system
CDISC SDTM Visualizations – Adverse Events

**Frequency of AEs**

- **BLOOD AND LYMPHATIC SYSTEMS:**
  - ALANINE AMINOTRANSFERASE...
  - ASPARTATE AMINOTRANSFERASE...
- **CARDIOVASCULAR SYSTEMS:**
  - BLOOD PRESSURE INCREASED...
- **GASTROINTESTINAL SYSTEMS:**
  - BLOOD GLUCOSE DECREASED...
- **ENDOCRINE DISORDERS:**
  - NEUROLOGICAL DISORDERS...
- **IMMUNE SYSTEM DISORDERS:**
  - INFECTION AND INFECTIOUS DISORDERS...
- **METAPOSSIS AND NUTRITIONAL SYSTEMS:**
  - METABOLISM AND NUTRITIONAL DISORDERS...
- **MUSCULOSKELETAL SYSTEMS:**
  - MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS...
- **REPRODUCTIVE SYSTEMS:**
  - REPRODUCTIVE SYSTEM AND BREAST DISORDERS...
- **RESPIRATORY SYSTEMS:**
  - NEUROLOGICAL DISORDERS...
- **SKIN AND SUBANITOUS TISSUE:**
  - SKIN AND SUBANITOUS TISSUE...
- **VASCULAR SYSTEMS:**
  - VASCULAR DISORDERS...

**Drill-Down: AE Subject Count by Term**

- **Dictionary-Derived Term:**
  - ALANINE AMINOTRANSFERASE...
  - ASPARTATE AMINOTRANSFERASE...
  - BLOOD PRESSURE INCREASED...
  - BLOOD GLUCOSE DECREASED...
  - NEUROPHIL COUNT INCREASE...
  - WHITE BLOOD CELL COUNT INCREASE...

**Drill-Down: Adverse Events by Summary Variable**

- **Dictionary-Derived Term:**
  - ALANINE AMINOTRANSFERASE...
  - ASPARTATE AMINOTRANSFERASE...
  - HEREDITARY ENZYMES...
  - BLOOD GLUCOSE INCREASED...
  - BLOOD PRESSURE INCREASED...
  - BLOOD CRITINE INCREASED...
  - BLOOD GLUCOSE DECREASED...
  - Q-REACTIVE PROTEIN INCREASED...
CDISC SDTM Visualizations – Subject Report

Select Event Types to display:
- AE
- Coded
- Disease Response
- Disposition
- DM Status
- Dose
- Lab
- MedHist
- Visit

Note: To drill down into the data of particular subjects in section 3, first add those patients to the Selected Subjects marking to populate the Subject List table, then mark the row from this table corresponding to the subject of interest.

Subject Details

AE: Non-Serious...
AE: Serious (Color = Severity)
CM: CONCOMITANT MEDICATION
DOSE
DS: DISPOSE...
DS: OTHER ...
DS: PROTOCOL MILESTONE
LB: HIGH NORMAL
LB: LOW NORMAL
VISIT

Subject List

Unique Subject Identifier

Data Editing:
- Selected Subjects
- dm: dm table
- Marking: Subject Report

Legend:
- LABS: High, High Panic, Low, Abnormal, Normal
- AEi: Mild(1), Moderate(2), Severe(3), (4), (5), Serious
- MH: Ongoing, During and/or After, Coincident, Before
- DSi: Randomized, Death/Withdrawn/Term
- RSi: PD, SD, TR, VGR, VPR, IC, LCR, CR, UCR, NO, UNK

Use slider to set Marker size.

Quick Mark:
- Active
- Screen Failure
- Ended

Data table: cm
Marking: Selected Subjects...
CDISC SDTM Visualizations – Subject Report

Subject Details

AE: Non-Serious (C... -
AE: Serious (Color = Severity)
CM: CONCOMITANT MEDICATION
DOSE
DS: DISPOSITION...
DS: OTHER EVENT
DS: PROTOCOL MILESTONE
LB: HIGH NORMAL
LB: LOW NORMAL
VISIT

<Encoded>: PRURITUS GENERALISED
<Encoded>: ALANINE AMINOTRANSFERASE INCREASED
<Encoded>: ASPARTATE AMINOTRANSFERASE INCREASED
<Encoded>: CITALOPRAM HYDROBROMIDE
<Encoded>: DEXLANSOPRAZOLE
<Encoded>: DIPHENHYDRAMINE HYDROCHLORIDE
<Encoded>: IRON TREATMENT
ADVERSE EVENT
LAST DOSE
INFORMED CONSENT OBTAINED
RANDOMIZED
ALP
ALT
AST
BILDIR
CMVIGGAB
EBGIGGAB
MPV
RDW
CREAT

Unique Subject Identifier: DEMO-291-0006
EventCategory: LB: LOW NORMAL
Event: CREAT
EventDetail: Day: -29, Date: 2012-09-04, Test: Creatinine: 0.6 mg/dL

DAY 1, Date: 2012-10-03
CDISC SDTM Visualizations – Labs

### Subject List

<table>
<thead>
<tr>
<th>Subject Identifier</th>
<th>Age</th>
<th>Sex</th>
<th>Race</th>
<th>Country</th>
<th>Subject Reference Start Datetime</th>
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</thead>
<tbody>
<tr>
<td>DEMO-001-0010</td>
<td>68</td>
<td>F</td>
<td>BLA</td>
<td>USA</td>
<td>25/07/2012</td>
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<tr>
<td>DEMO-033-0018</td>
<td>33</td>
<td>F</td>
<td>WHITE</td>
<td>USA</td>
<td>26/12/2012</td>
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<tr>
<td>DEMO-009-0006</td>
<td>42</td>
<td>F</td>
<td>BLA</td>
<td>USA</td>
<td>15/09/2012</td>
</tr>
<tr>
<td>DEMO-145-0004</td>
<td>49</td>
<td>F</td>
<td>WHITE</td>
<td>USA</td>
<td>30/01/2013</td>
</tr>
<tr>
<td>DEMO-183-0002</td>
<td>47</td>
<td>F</td>
<td>WHITE</td>
<td>USA</td>
<td>17/01/2013</td>
</tr>
<tr>
<td>DEMO-101-0004</td>
<td>70</td>
<td>F</td>
<td>BLA</td>
<td>USA</td>
<td>03/01/2012</td>
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<tr>
<td>DEMO-210-0008</td>
<td>46</td>
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<td>WHITE</td>
<td>USA</td>
<td>13/09/2012</td>
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<tr>
<td>DEMO-201-0006</td>
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<td>F</td>
<td>WHITE</td>
<td>USA</td>
<td>03/09/2012</td>
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<td>DEMO-403-0002</td>
<td>28</td>
<td>F</td>
<td>WHITE</td>
<td>USA</td>
<td>04/09/2012</td>
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<tr>
<td>DEMO-404-0004</td>
<td>76</td>
<td>F</td>
<td>WHITE</td>
<td>USA</td>
<td>28/11/2012</td>
</tr>
</tbody>
</table>

### Max xULN Lab Values - Selected Subjects

<table>
<thead>
<tr>
<th>Unique Subject Identifier</th>
<th>ALT(ULN)</th>
<th>BILI(mg/dL)</th>
<th>DILI Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>DEMO-001-0010</td>
<td>1.38</td>
<td>0.32</td>
<td>Below CLC</td>
</tr>
<tr>
<td>DEMO-005-0008</td>
<td>1.39</td>
<td>0.46</td>
<td>Below CLC</td>
</tr>
<tr>
<td>DEMO-183-0002</td>
<td>1.15</td>
<td>0.21</td>
<td>Below CLC</td>
</tr>
<tr>
<td>DEMO-191-0002</td>
<td>0.42</td>
<td>0.25</td>
<td>Below CLC</td>
</tr>
<tr>
<td>DEMO-403-0004</td>
<td>1.67</td>
<td>0.35</td>
<td>Below CLC</td>
</tr>
<tr>
<td>DEMO-404-0004</td>
<td>2.48</td>
<td>0.66</td>
<td>Below CLC</td>
</tr>
<tr>
<td>DEMO-523-0001</td>
<td>2.54</td>
<td>0.67</td>
<td>Below CLC</td>
</tr>
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<td>DEMO-565-0007</td>
<td>1.85</td>
<td>0.35</td>
<td>Below CLC</td>
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<tr>
<td>DEMO-540-0003</td>
<td>0.67</td>
<td>0.29</td>
<td>Below CLC</td>
</tr>
<tr>
<td>DEMO-727-0019</td>
<td>0.84</td>
<td>0.44</td>
<td>Below CLC</td>
</tr>
<tr>
<td>DEMO-767-0005</td>
<td>0.94</td>
<td>0.21</td>
<td>Below CLC</td>
</tr>
</tbody>
</table>

### Lab Results - Selected Subjects

To drill down into the data of particular subjects in section 3, first add those patients to the Selected Subjects marking to populate the Subject List table; then mark the row from this table corresponding to the subject of interest.
CDISC SDTM Visualizations – Hy’s Law

NOTE: The BILI (Max ULN) vs ALT (Max ULN) below shows MAXIMUM ULN values IRRESPECTIVE of visit. Any possible Hy’s law candidate should be verified against the Elevated Values Table to the right. That table shows the visits where the elevated ALT and BILI occurred.

Hy’s Quadrant: ALT greater than or equal to 3 x ULN and BILI greater than or equal to 2 x ULN
Temple’s Corollary: ALT greater than or equal to 3 x ULN and BILI less than 2 x ULN
Elevated BILI: ALT less than 3 x ULN and BILI greater than or equal to 2 x ULN

Data table: LabMaxValues

Marking:
- Selected Subject
- Selected Value

Expressing:

Unique Subject Identifier
DEMO-030-00015
100.00
100.01
VISIT 4
UNSH C
28.00
42.00

ALT = 3
BILI = 2

Study Day of Specimen Collection
True
False
True

Drill-Down: Selected Labs over Study Timeline

Elevated Values Table (shows elevated ALT/BILI ULN values at common visit)
CDISC SDTM Visualizations – Accessing Risk
CFAST Therapeutic Area Support

“CFAST is an initiative formed to accelerate clinical research and medical product development by creating and maintaining data standards, tools and methods for conducting research in therapeutic areas that are important to public health. CFAST was initiated as a partnership between CDISC and the Critical Path Institute (C-Path).”

<table>
<thead>
<tr>
<th>Project</th>
<th>Publication Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alzheimer’s Disease v1</td>
<td>September 9, 2011</td>
</tr>
<tr>
<td>Tuberculosis v1</td>
<td>June 29, 2012</td>
</tr>
<tr>
<td>Pain v1</td>
<td>August 7, 2012</td>
</tr>
<tr>
<td>Virology v1</td>
<td>December 6, 2012</td>
</tr>
<tr>
<td>Parkinson’s Disease v1</td>
<td>December 18, 2012</td>
</tr>
<tr>
<td>Polycystic Kidney Disease v1</td>
<td>February 26, 2013</td>
</tr>
<tr>
<td>Asthma v1</td>
<td>November 26, 2013</td>
</tr>
<tr>
<td>Alzheimer’s Disease v2</td>
<td>December 16, 2013</td>
</tr>
<tr>
<td>Multiple Sclerosis v1</td>
<td>May 2, 2014</td>
</tr>
<tr>
<td>Diabetes v1 (ADaM Supplement)</td>
<td>September 11, 2014 (December 18, 2015)</td>
</tr>
<tr>
<td>Cardiovascular Endpoints v1</td>
<td>October 17, 2014</td>
</tr>
<tr>
<td>Influenza v1</td>
<td>November 25, 2014</td>
</tr>
<tr>
<td>QT Studies v1</td>
<td>December 12, 2014</td>
</tr>
<tr>
<td>Chronic Hepatitis C Virus v1</td>
<td>May 8, 2015</td>
</tr>
<tr>
<td>Schizophrenia v1</td>
<td>June 9, 2015</td>
</tr>
<tr>
<td>Dyslipidemia v1</td>
<td>June 19, 2015</td>
</tr>
<tr>
<td>Virology v2</td>
<td>September 30, 2015</td>
</tr>
<tr>
<td>Traumatic Brain Injury v1</td>
<td>December 14, 2015</td>
</tr>
<tr>
<td>COPD v1</td>
<td>January 26, 2016</td>
</tr>
<tr>
<td>Tuberculosis v2</td>
<td>February 26, 2016</td>
</tr>
<tr>
<td>Breast Cancer v1</td>
<td>May 16, 2016</td>
</tr>
<tr>
<td>Rheumatoid Arthritis v1</td>
<td>November 14, 2016</td>
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<tr>
<td>Kidney Transplant</td>
<td>October 31, 2016</td>
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<tr>
<td>Major Depressive Disorder v1</td>
<td>December 5, 2016</td>
</tr>
<tr>
<td>Diabetic Kidney Disease v1</td>
<td>December 13, 2016</td>
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<tr>
<td>Pain v1.1 (update)</td>
<td>December 13, 2016</td>
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<tr>
<td>Ebola v1</td>
<td>December 19, 2016</td>
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<tr>
<td>Malaria v1</td>
<td>January 9, 2017</td>
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<tr>
<td>Schizophrenia v1.1</td>
<td>May 3, 2017</td>
</tr>
<tr>
<td>Prostate Cancer v1.0</td>
<td>July 10, 2017</td>
</tr>
</tbody>
</table>

1 Source: www.cdisc.org/cfast-0
Cross-functional leadership team with clear accountabilities that address strategic, operational, medical and scientific challenges.

Drive all PPD rare disease and pediatric-related activities.

Leverage expertise to drive new approaches to trial delivery.

By therapeutic area, 516 studies as of March 2017:

- Circulatory System, 96
- Blood, Blood-forming Organs, 46
- Symptoms, Signs, Ill-defined Conditions, 8
- Skin and Subcutaneous Tissue, 11
- Respiratory System, 37
- Perinatal Conditions, 10
- Other, 10
- Nervous System and Sense Organs, 75
- Neoplasms, 47
- Musculoskeletal System & Connective Tissue, 9
- Multiple (ISS/ISE), 7
- Infectious & Parasitic Diseases, 65
- General Medicine, 47
- Digestive System, 15
- Miscellaneous, 10
- Endocrine, Nutritional/Metabolic & Immunity, 23

HELPING DELIVER LIFE-CHANGING THERAPIES
Enhanced Therapeutic Area Support

- We established Therapeutic Area (TA) working groups to enhance the Preclarus® PDD specifically for TAs based on the CFAST therapeutic area user guides (TAUGs), for example:

  - **Oncology** – Disease response assessments and CTCAE
  - **Cardiovascular** – Identification of MACE events
  - **Neurology** – Enhanced questionnaire support
  - **Vaccines** – Solicited AEs and reactogenicity
  - **Ophthalmology** – Recognition of study and non-study eye
Delivering Visualizations – Oncology
Delivering Visualizations – Oncology

Subject Swimmer Plot

ACTTTR

Planned Arm Code | Maximum Study Day for Subject Report | Unique Subject Identifier

840.00 - ONCDEM01-01...
689.00 - ONCDEM01-09...
574.00 - ONCDEM01-06...
514.00 - ONCDEM01-00...
478.00 - ONCDEM01-07...
447.00 - ONCDEM01-02...
398.00 - ONCDEM01-00...
378.00 - ONCDEM01-08...
369.00 - ONCDEM01-08...
353.00 - ONCDEM01-00...
348.00 - ONCDEM01-01...
342.00 - ONCDEM01-02...
330.00 - ONCDEM01-03...
318.00 - ONCDEM01-10...
314.00 - ONCDEM01-02...
268.00 - ONCDEM01-00...
235.00 - ONCDEM01-07...
232.00 - ONCDEM01-10...
223.00 - ONCDEM01-10...
211.00 - ONCDEM01-03...
203.00 - ONCDEM01-09...
180.00 - ONCDEM01-07...
119.00 - ONCDEM01-07...
101.00 - ONCDEM01-01...
Delivering Visualizations – Vaccines
CDISC SDTM Challenges Encountered

Identifying data that has changed between SDTM runs
- When comparing data across two runs of SDTM, sequence variables (xxSEQ) are often re-assigned.

Presenting data not yet standardized within SDTM, e.g.
- Pulmonary Function Tests (PFTs), RE domain not yet approved
- American Diabetes Association Classification of Hypoglycemia

Accounting for accepted variations in SDTM, e.g.
- Displaying captured relationships, i.e. using RELREC

SDTM inconsistencies, e.g.
- EXTRT change from “Name of Actual Treatment” to “Name of Treatment”
Delivering CDISC SDTM Visualizations

+ PPD’s Preclarus® Patient Data Dashboard (PDD) is a dynamic and visualization based view of CDISC SDTM data for ongoing review and monitoring.
+ **Scalable:** Out-of-the-box data review tool for any SDTM study
+ **Comprehensive and Intuitive:** Centrally developed by experts
+ **Cost effective:** No study specific customisation required
+ **Quick to deploy:** Simply upload SDTM into the system

+ Using SDTM Standards we have successfully deployed:
  + Interactive visualisations across over 30 SDTM domains so far:
  + 120 visualisations across over 40 individual pages
  + Implement on over 70 studies across 10 clients and rising, for example:
    + Deployed for safety review/ trending
    + Deployed for dose escalation support
    + Deployed for identifying data issues
Contact Information

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