Novo Nordisk at a glance

- More than 27,000 employees in 81 countries
- A world leader in diabetes care since 1923
- Also leading positions in:
  - Haemostasis management
  - Growth hormone therapy
  - Hormone replacement therapy
- Total net turnover (2008): 8.64 billion USD
- Committed to financial, environmental and social results
CDW and CDW Operations

We develop standard programs for generating derived data and output for clinical documentation.

We maintain and develop the data model.

We do mapping from OC to CDW and maintain standards (generic trial designs, codes and code lists).

Clinical Data Warehouse

**Analysis platform - SAS DD**
- Std program library
- Data set creation
- Data set creation
- Derived Data Marts

**CDW Operation Application**
- Meta Data Management
- Source Data Mapping
- Data transfer and Admin

**Data Repository**

**Clinical Data Repository**

**Meta Data Repository**

**Clinical Applications**
- IMPACT
- Oracle Clinical
- Trial Meta data
- Clinical Data

Global data and meta data repository holding a data model ensuring alignment to the FDA data standard, CDISC

Global statistical analysis platform with audit trail for generating output reports.

We develop standard programs for generating derived data and output for clinical documentation.

We maintain and develop the data model.
Metadata

• What is metadata?
• Metadata is data about data
• Example: For visit we can have:
  • a visit code
  • different labels to use in reports and plots
  • information of planned time
  • information of allowed visit windows
  • and a lot more
Sources for metadata

**Internal standards**
- Std CRFs
- Oracle Clinical code lists
- Mapping Standards
- Protocol Metadata Template
- Std templates and reports
- Business Rules

**External standards**
- CDISC Standards
Data is not limited to Clinical Data

Cross-organisational Clinical Data Warehouse

Internal and External Data Standards

Clinical Data

Global Metadata

Trial Specific Metadata

Business Rules and Data Decisions
Global Metadata

• Defined across all project and trials

• Generic Trial Designs
  • Trial arms
  • Branches
  • Epochs
  • Elements
Global Metadata

Define Generic Trial Design

Add Arms, Epochs, Elements and Branches, and define relations between epochs, arms and elements

<table>
<thead>
<tr>
<th>Arm</th>
<th>Branch</th>
<th>Screening Epoch</th>
<th>Wash-out Epoch 1</th>
<th>Treatment Epoch 1</th>
<th>Wash-out Epoch 2</th>
<th>Treatment Epoch 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arm 1</td>
<td>Arm 1</td>
<td>Screening</td>
<td>✔️</td>
<td>✔️ Treatment A</td>
<td>✔️ Wash-out</td>
<td>✔️ Treatment B</td>
</tr>
<tr>
<td>Arm 2</td>
<td>Arm 2</td>
<td>Screening</td>
<td>✔️</td>
<td>✔️ Treatment B</td>
<td>✔️ Wash-out</td>
<td>✔️ Treatment A</td>
</tr>
</tbody>
</table>

No. of All Elements: 5
No. of Treatment Elements: 2
No. of All Epochs: 6
No. of Treatment Epochs: 2
No. of Trial Arms: 2
Status: Active
Global Metadata

• Topic codes
  • Units
  • Display formats
  • Unit conversion metadata
  • Labels

• Site and Investigator metadata

• Code lists
Trial Specific Metadata

- Defined within the trial
- Trial Design
- Visits
  - Association to Oracle Clinical visit
  - Labels
  - Planned time
  - Windows
  - Visit type
Trial Specific Metadata

- Trial Flowchart
  - Shows planned findings
  - Contains connection between topic codes and visits
  - Allocation of Business Rules for each topic code/visit combination
# Trial Specific Metadata

## Flowchart

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Visit Short Label</th>
<th>V1 Screening visit</th>
<th>V2 Baseline/Randomisation visit</th>
<th>V3 Treatment visit</th>
<th>V4 Treatment visit</th>
<th>V5 Treatment visit</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EFFICACY</strong></td>
<td>Insulin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Basal Insulin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bolus Insulin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Premix insulin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glucose metabolism</td>
<td>Fasting plasma glucose level</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Blood HbA1c</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Self measured plasma glucose</td>
<td>Self Measured Plasma Glucose level</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td><strong>EXCLUSION CRITERIA</strong></td>
<td>Exclusion criteria</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Clin Sign Active Diseases</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Positive HIV Antibodies</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Clin Sign Abnorm LAB Screening Tests</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hepatitis B Antigen or C Antibody “+”</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Impaired hepatic ASAT/ALAT &gt; 2.5 normal</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Predict change eating, exercise habits</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Disease/condi interfering with trial</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mental Incapacity, Unwillingness</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Proliferative Retinopathy or Maculopathy</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Impaired Renal fun MF</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cardiac problems within 12 months</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cancer (except basal/squamous cell skin)</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Severe hypertension</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Allergy To Trial Products</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hypoglycaemia Unawareness/Hosp</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Trial Specific Metadata

Collection Attributes

Flowchart Group: Glucose metabolism
Assessment: Blood HbA1c
Visit ID: 10
Visit Short Label: V1

Treatment Allocation: Current Visit
Assessment Type: Baseline Assessment
Mandatory for PP Population: 
Qualify for FAS Population: 
Pre Visit Date Time Window: Days
Post Visit Date Time Window: Days
Pre First Drug Date Time Window: Days
Post First Drug Date Time Window: Days
Pre Last Drug Date Time Window: Days
Post Last Drug Date Time Window: Days
Retest Rule: 
Missing Finding Value Rule: 
Visit Reallocation Rule: 
Missing Finding Date Rule: 
Missing Finding Time Rule: 

changing diabetes

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Trial Specific Metadata

Assessment Attributes

Flowchart Group: Efficacy
Assessment: Blood HbA1c
Finding Topic Code: HBA1C_BLOOD

Protocol Attributes

Planned Finding Group: Glucose metabolism
Planned Finding Sub Group: 
Profile Name: 

Statistical Attributes

Lower Limit Type: 
Lower Limit Value: 
Lower Limit Rule: 
Lower Limit Value Censored: 
Lower Limit Unit: 

changing diabetes

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Data derivations and enrichments

- Performed by the DVE Framework

- Program complex composed of a shell and a lot of building block components

- Purpose:
  - Conversions (date, time, character to numeric)
  - Blinding (subject level, fake randomisation, blinded treatment, specific topic codes)
  - Treatment allocation
  - Populations, flags and derived variables
  - And a lot more ..
Standard Analysis Reporting

- Standard Program Library
  - Macros
  - Tables
  - Figures
  - Listings
Metadata in Standard Analysis Reporting UI’s
Metadata in Standard Analysis Reporting UI’s

- `ddm.plnd_trl_arm`
- `ddm.plnd_trl_branch_arm`
- `ddm.plnd_trl_elem`
Metadata in Standard Analysis Reporting UI’s

- `ddm.plnd_trl_arm`
- `ddm.plnd_trl_branch_arm`
- `ddm.plnd_trl_elem`

- `ddm.plnd_flowch_item_coll`

  Topic Code
  Visit ID
Metadata in Standard Analysis Reporting UI’s
# How are the metadata displayed

## Summary of Blood pressure (Systolic) (mmHg) by Visit and Treatment

<table>
<thead>
<tr>
<th></th>
<th>BI Amp 50</th>
<th>BI Amp 70</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>/70</td>
<td>/50</td>
<td></td>
</tr>
</tbody>
</table>

### Number of Subjects
- 37 for BI Amp 50
- 37 for BI Amp 70
- 74 Total

### Topic codes and units
- Population (and sub-group)
- Treatment metadata
- Visit metadata
- Statistics
- Display formats

### Data Table

<table>
<thead>
<tr>
<th>Visit</th>
<th>N</th>
<th>Mean (SD)</th>
<th>Median</th>
<th>Min : Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>BI Amp</td>
<td>37</td>
<td>144 (16)</td>
<td>145</td>
<td>115 : 175</td>
</tr>
<tr>
<td>6</td>
<td>37</td>
<td>144 (16)</td>
<td>145</td>
<td>115 : 175</td>
</tr>
<tr>
<td>V12</td>
<td>37</td>
<td>137 (15)</td>
<td>140</td>
<td>110 : 185</td>
</tr>
<tr>
<td>V14</td>
<td>37</td>
<td>133 (15)</td>
<td>135</td>
<td>100 : 160</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Change (absolute) from Baseline to V14</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
</tr>
<tr>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Median</td>
</tr>
<tr>
<td>Min : Max</td>
</tr>
</tbody>
</table>
How much is metadata controlled?

Summary of Blood pressure (Systolic) (mmHg) by Visit and Treatment.

<table>
<thead>
<tr>
<th></th>
<th>All Subjects</th>
<th>BI A mp 50 / 70</th>
<th>BI A mp 70 / 50</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Subjects</td>
<td>37</td>
<td>37</td>
<td>37</td>
<td>74</td>
</tr>
<tr>
<td>Screen</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>142 (16)</td>
<td>144 (14)</td>
<td>143 (15)</td>
<td>143</td>
</tr>
<tr>
<td>Median</td>
<td>145</td>
<td>145</td>
<td>145</td>
<td>145</td>
</tr>
<tr>
<td>Min : Max</td>
<td>115 ; 175</td>
<td>120 ; 171</td>
<td>115 ; 175</td>
<td>115</td>
</tr>
<tr>
<td>Baseline</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>143 (14)</td>
<td>144 (15)</td>
<td>142 (15)</td>
<td>142</td>
</tr>
<tr>
<td>Median</td>
<td>143</td>
<td>143</td>
<td>143</td>
<td>143</td>
</tr>
<tr>
<td>Min : Max</td>
<td>113 ; 166</td>
<td>116 ; 172</td>
<td>113 ; 172</td>
<td>113</td>
</tr>
<tr>
<td>V6</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>141 (13)</td>
<td>144 (14)</td>
<td>143 (15)</td>
<td>143</td>
</tr>
<tr>
<td>Median</td>
<td>146</td>
<td>146</td>
<td>146</td>
<td>146</td>
</tr>
<tr>
<td>Min : Max</td>
<td>113 ; 170</td>
<td>109 ; 173</td>
<td>109 ; 173</td>
<td>109</td>
</tr>
<tr>
<td>V12</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>137 (15)</td>
<td>141 (14)</td>
<td>139 (15)</td>
<td>139</td>
</tr>
<tr>
<td>Median</td>
<td>140</td>
<td>140</td>
<td>140</td>
<td>140</td>
</tr>
<tr>
<td>Min : Max</td>
<td>110 ; 185</td>
<td>110 ; 176</td>
<td>110 ; 185</td>
<td>110</td>
</tr>
<tr>
<td>V14</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>137 (12)</td>
<td>141 (14)</td>
<td>138 (13)</td>
<td>138</td>
</tr>
<tr>
<td>Median</td>
<td>136</td>
<td>140</td>
<td>139</td>
<td>139</td>
</tr>
<tr>
<td>Min : Max</td>
<td>113 ; 165</td>
<td>108 ; 173</td>
<td>108 ; 173</td>
<td>108</td>
</tr>
<tr>
<td>Change (absolute) from Baseline to V14</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>8 (19)</td>
<td>9 (12)</td>
<td>9 (13)</td>
<td>9</td>
</tr>
<tr>
<td>Median</td>
<td>10</td>
<td>10</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>Min : Max</td>
<td>-18 ; 95</td>
<td>-10 ; 40</td>
<td>-18 ; 45</td>
<td>-18</td>
</tr>
</tbody>
</table>
Conclusion

The use of metadata and standard programs have given us a lot of benefits:

- Business Rules and Data Decisions are defined in a standardised way
- Business Rules and Data Decisions no longer embedded in SAS program code
- By separating the definition and the implementation/use of the business rules it is possible to make enrichment and derivations data driven
- Data driven data checking
- Data driven use of business rules and application of data decisions
- Transparency and easy documentation
- Consistent presentation of data