

**Florence Somers**

Practice Manager  
Statistical Programming  
Business & Decision Life Sciences -  
Brussels

Tel +32 2 774 11 00  
Fax +32 2 774 11 99  
Mobile +32 491 15 37 47  
[florence.somers@businessdecision.com](mailto:florence.somers@businessdecision.com)

**Andrew Winkler**

Sr. Principal, R&D  
Business & Decision Life Sciences -  
North America

Tel +1 919-428-3592  
[andrew.winkler@businessdecision.com](mailto:andrew.winkler@businessdecision.com)

[www.businessdecision-lifesciences.com](http://www.businessdecision-lifesciences.com)

## Traceability between the clinical database and analysis datasets for a submission



**DRIVE YOUR PERFORMANCE**

# Topics



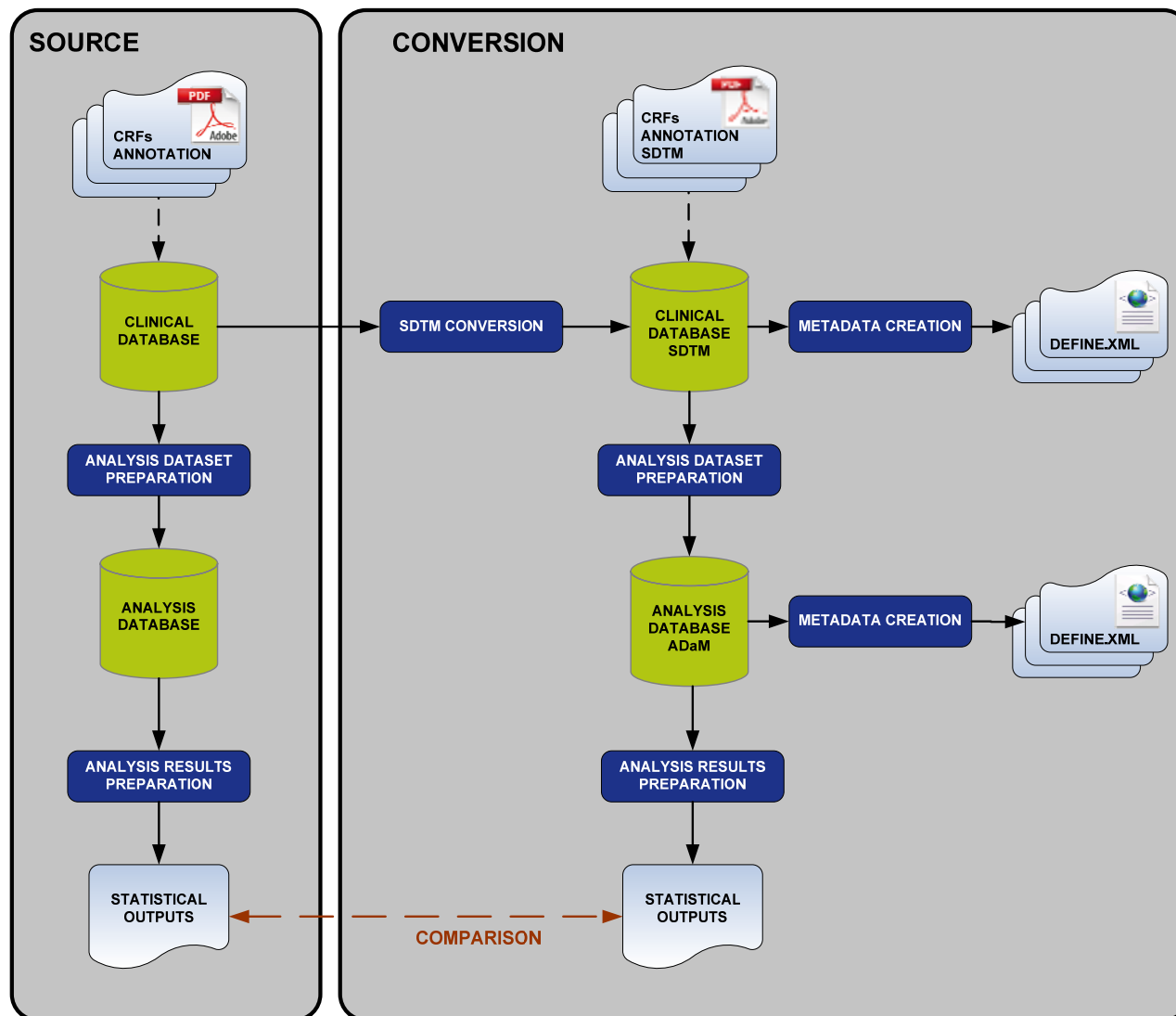
# Topics



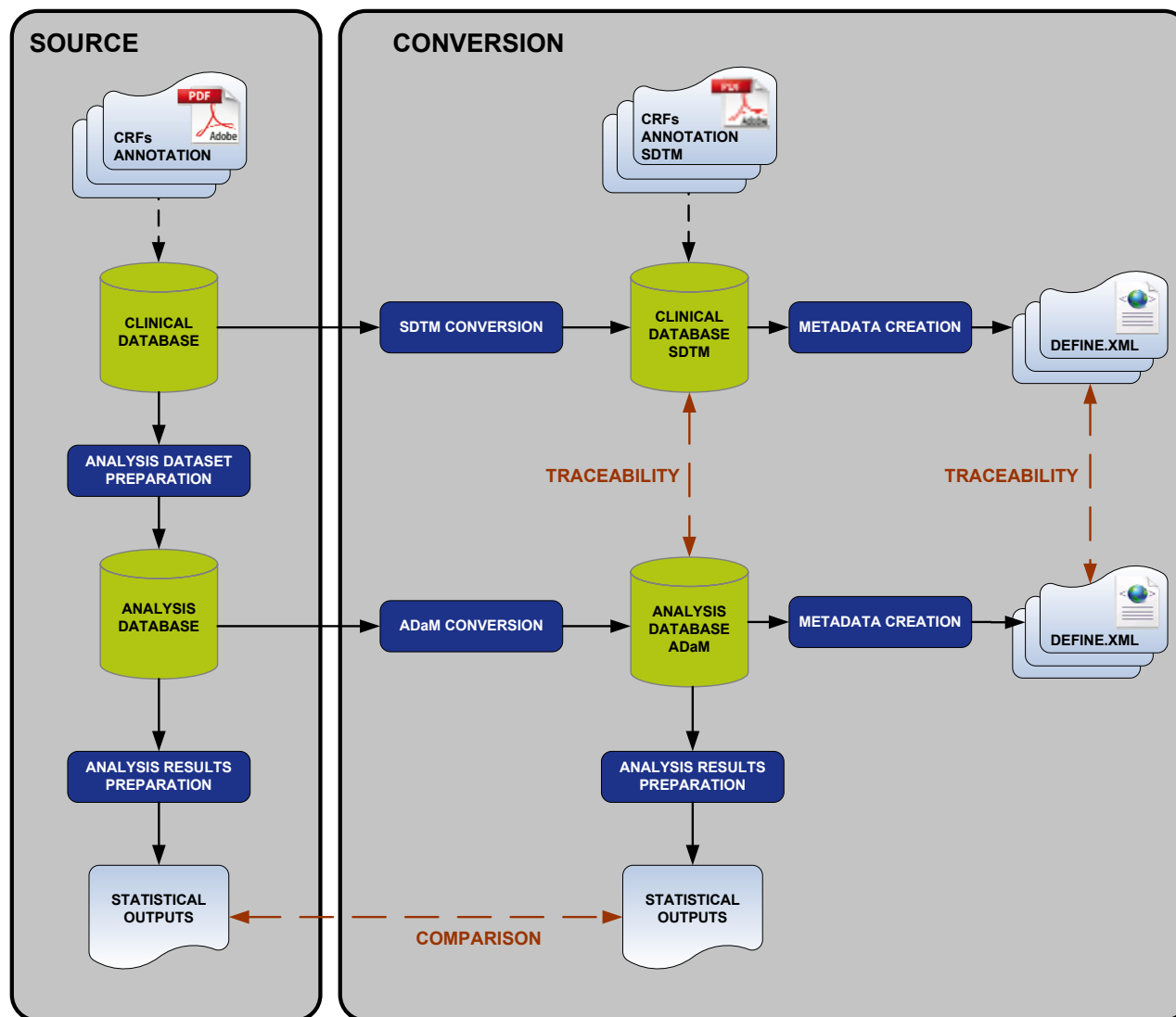
## SDTM/ADaM adoption by FDA

- SDTM is expected to be « required for FDA submission » within 2 years
  - CDER is accepting SDTM submissions
  - CBER is accepting SDTM submissions since May 2010
  - CDRH interest is rising, CDISC SDTM team has formed a medical devices subteam
- FDA CDER:
  - Requesting sponsors to submit in SDTM format
  - Encouraging sponsors to submit in ADaM format
- Continuous FDA pilot projects, both CDER and CBER

# Implementation approaches: strategy 1



## Implementation approaches: strategy 2



## Traceability SDTM and ADaM

- Understanding relationship between the analysis results, the analysis datasets and the SDTM domains
- Establishing the path between an element and its immediate predecessor
- Two levels:
  - Metadata traceability
    - Relationship between an analysis result and analysis dataset(s)
    - Relationship of the analysis variable to its source dataset(s) and variable(s)
  - Data point traceability
    - Predecessor record(s)

# Traceability SDTM and ADaM

Table 1 Demographic Data - Per-Protocol

|                                          | Treatment 1 | Treatment 2  |
|------------------------------------------|-------------|--------------|
| Baseline body mass index (BMI) [kg/m**2] |             |              |
| N                                        | 167         | 167          |
| Mean                                     | 29.06       | 29.04        |
| SD                                       | 4.84        | 4.80         |
| Min                                      | 20.3        | 16.0         |
| Median                                   | 28.69       | 28.47        |
| Max                                      | 40.1        | 41.2         |
| Baseline BMI (categorical) [N (%)]       |             |              |
| <25 kg/m**2                              | 41 ( 24.6%) | 71 ( 21.1%)  |
| 25-<30 kg/m**2                           | 60 ( 35.9%) | 130 ( 38.7%) |
| >=30 kg/m**2                             | 66 ( 39.5%) | 135 ( 40.2%) |

## • Patient Demographics - Part I

Patient X5 Page 4 (Demo\_V1a for Visit 1a) Page 1 of 1.

Visit Date 11-Dec-2007 Blank Comment

PATIENT DEMOGRAPHICS - Part I **DSCAT = "PROTOCOL MILESTONE"**

Informed consent was obtained on **DSSTDT**

**DSTERM / DSDECD**

Gender **SEX** 1 = male, 2 = female

Date of birth **BRTHDTC** Age **AGEU** years (Age is automatically calculated when screen is saved and closed)

Height  cm

Weight  kg

Waist circumference  cm

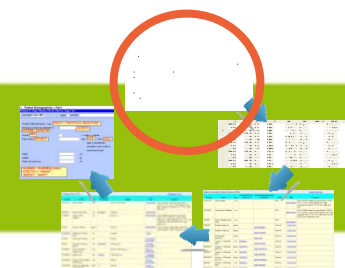
**VSORRES / VSORRESU where VSTESTCD = "HEIGHT", "WEIGHT", "WAIST"**

|    | STUDYID   | USUBJID          | SUBJID | BMI                       | BMGR1 | BMGRIN | BMGR2            | BMGR2N |
|----|-----------|------------------|--------|---------------------------|-------|--------|------------------|--------|
| 2  | 9999-0001 | 9999-0001-000001 | 000001 | 27.77777778 <30 kg/m**2   |       |        | 1 25-<30 kg/m**2 | 2      |
| 3  | 9999-0001 | 9999-0001-000002 | 000002 | 25.50361502 <30 kg/m**2   |       |        | 1 25-<30 kg/m**2 | 2      |
| 4  | 9999-0001 | 9999-0001-000003 | 000003 | 26.175194521 <30 kg/m**2  |       |        | 1 25-<30 kg/m**2 | 2      |
| 5  | 9999-0001 | 9999-0001-000004 | 000004 | 35.15625 >=30 kg/m**2     |       |        | 2 >=30 kg/m**2   | 3      |
| 6  | 9999-0001 | 9999-0001-000005 | 000005 | 30.96958131 >=30 kg/m**2  |       |        | 2 >=30 kg/m**2   | 3      |
| 7  | 9999-0001 | 9999-0001-000006 | 000006 | 34.697162916 >=30 kg/m**2 |       |        | 2 >=30 kg/m**2   | 3      |
| 8  | 9999-0001 | 9999-0001-000007 | 000007 | 25.85646281 <30 kg/m**2   |       |        | 1 25-<30 kg/m**2 | 2      |
| 9  | 9999-0001 | 9999-0001-000008 | 000008 | 30.103806228 >=30 kg/m**2 |       |        | 2 >=30 kg/m**2   | 3      |
| 10 | 9999-0001 | 9999-0001-000009 | 000009 | 32.28962693 >=30 kg/m**2  |       |        | 2 >=30 kg/m**2   | 3      |
| 11 | 9999-0001 | 9999-0001-000010 | 000010 | 28.876133787 <30 kg/m**2  |       |        | 1 25-<30 kg/m**2 | 2      |
| 12 | 9999-0001 | 9999-0001-000011 | 000011 | 29.372287383 <30 kg/m**2  |       |        | 1 25-<30 kg/m**2 | 2      |
| 13 | 9999-0001 | 9999-0001-000012 | 000012 | 26.714862608 <30 kg/m**2  |       |        | 1 25-<30 kg/m**2 | 2      |
| 14 | 9999-0001 | 9999-0001-000013 | 000013 | 32.718619889 >=30 kg/m**2 |       |        | 2 >=30 kg/m**2   | 3      |
| 15 | 9999-0001 | 9999-0001-000014 | 000014 | 28.719723193 <30 kg/m**2  |       |        | 1 25-<30 kg/m**2 | 2      |
| 16 | 9999-0001 | 9999-0001-000015 | 000015 | 32.270420377 >=30 kg/m**2 |       |        | 2 >=30 kg/m**2   | 3      |

| Variable | Label                                    | Type    | Controlled Terminology  | Origin             | Role             | Comment                                                                                                                                                                           |
|----------|------------------------------------------|---------|-------------------------|--------------------|------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| STUDYID  | Study Identifier                         | text    | Protocol, CRF Page 1    | Protocol           | IDENTIFIER       | The STUDYID variable has a fixed format: 'XXXX-YYYY', where 'XXXX' indicates the 4-digit compound code and the 'YYYY' the 4-digit study code.                                     |
| DOMAIN   | Domain Abbreviation                      | text    | DOMAIN                  | Assigned           | IDENTIFIER       |                                                                                                                                                                                   |
| USUBJID  | Unique Subject Identifier                | text    | Protocol                | Protocol           | IDENTIFIER       | The USUBJID variable has a fixed format: 'XXXX-YYYY-ZZZZZ', where 'XXXX' indicates the 4-digit compound code, 'YYYY' the 4-digit study code and 'ZZZZZ' the 5-digit patient code. |
| VSEQ     | Sequence Number                          | integer | Derived                 | Derived            | IDENTIFIER       |                                                                                                                                                                                   |
| VSTESTCD | Visit Sign Test Short Name               | text    | Assigned                | Assigned           | TOPIC            |                                                                                                                                                                                   |
| VSTEST   | Visit Sign Test Name                     | text    | Derived                 | Derived            | ANALYSIS         |                                                                                                                                                                                   |
| VSPIN    | Visit Sign Position of Subject           | text    | CRF Page 12             | RECORD QUALIFIER   | ANALYSIS         |                                                                                                                                                                                   |
| VSORRES  | Result or Finding in Original Units      | text    | Derived, CRF Page 2, 12 | RESULT QUALIFIER   | ANALYSIS         |                                                                                                                                                                                   |
| VSORRESU | Original Units                           | text    | CRF Page 2, 12          | VARIABLE QUALIFIER | ANALYSIS         |                                                                                                                                                                                   |
| VSTESTSC | Character Result Finding in Std Format   | text    | Derived                 | RESULT QUALIFIER   | ANALYSIS         |                                                                                                                                                                                   |
| VSTESTSN | Numeric Result Finding in Standard Units | float   | 3.1                     | Derived            | RESULT QUALIFIER |                                                                                                                                                                                   |

| Variable | Label                            | Type    | Controlled Terminology | Computation, Algorithm or Method | Origin  | Role       | Comment                                                                                                                                                                           |
|----------|----------------------------------|---------|------------------------|----------------------------------|---------|------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| STUDYID  | Study Identifier                 | text    |                        |                                  | DM      | IDENTIFIER | The STUDYID variable has a fixed format: 'XXXX-YYYY', where 'XXXX' indicates the 4-digit compound code and the 'YYYY' the 4-digit study code.                                     |
| USUBJID  | Unique Subject Identifier        | text    |                        |                                  | DM      | IDENTIFIER | The USUBJID variable has a fixed format: 'XXXX-YYYY-ZZZZZ', where 'XXXX' indicates the 4-digit compound code, 'YYYY' the 4-digit study code and 'ZZZZZ' the 5-digit patient code. |
| SUBJID   | Subject Identifier for the Study | text    |                        |                                  | DM      | IDENTIFIER |                                                                                                                                                                                   |
| HEIGHT   | Baseline Height (cm)             | integer |                        | ADSL HEIGHT                      | Derived | ANALYSIS   |                                                                                                                                                                                   |
| WEIGHT   | Baseline Weight (kg)             | integer |                        | ADSL WEIGHT                      | Derived | ANALYSIS   |                                                                                                                                                                                   |
| BMI      | Baseline BMI (kg/m**2)           | integer |                        | ADSL BMI                         | Derived | ANALYSIS   |                                                                                                                                                                                   |
| BMGR1    | Category 1 of Baseline BMI       | text    | BMGR1L                 | ADSL BMGR1                       | Derived | ANALYSIS   |                                                                                                                                                                                   |
| BMGRIN   | Category 1 of Baseline BMI, (N)  | integer | BMGRIN                 | ADSL BMGRIN                      | Derived | ANALYSIS   |                                                                                                                                                                                   |
| BMGR2    | Category 2 of Baseline BMI       | text    | BMGR2L                 | ADSL BMGR2                       | Derived | ANALYSIS   |                                                                                                                                                                                   |
| BMGR2N   | Category 2 of Baseline BMI, (N)  | integer | BMGR2N                 | ADSL BMGR2N                      | Derived | ANALYSIS   |                                                                                                                                                                                   |
| BMGR3    | Category 3 of Baseline BMI       | text    | BMGR3L                 | ADSL BMGR3                       | Derived | ANALYSIS   |                                                                                                                                                                                   |
| BMGR3N   | Category 3 of Baseline BMI, (N)  | integer | BMGR3N                 | ADSL BMGR3N                      | Derived | ANALYSIS   |                                                                                                                                                                                   |

# Traceability SDTM and ADaM

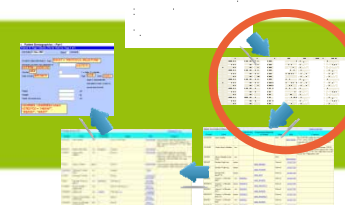


- Analysis Results

Table 1 Demographic Data - Per-Protocol

|                                          | Treatment 1 | Treatment 2  |
|------------------------------------------|-------------|--------------|
| Baseline body mass index (BMI) [kg/m**2] |             |              |
| N                                        | 167         | 167          |
| Mean                                     | 29.08       | 29.04        |
| SD                                       | 4.84        | 4.80         |
| Min                                      | 20.3        | 16.0         |
| Median                                   | 28.69       | 28.47        |
| Max                                      | 40.1        | 41.2         |
| Baseline BMI (categorical) [N (%)]       |             |              |
| <25 kg/m**2                              | 41 ( 24.6%) | 71 ( 21.1%)  |
| 25-<30 kg/m**2                           | 60 ( 35.9%) | 130 ( 38.7%) |
| >=30 kg/m**2                             | 66 ( 39.5%) | 135 ( 40.2%) |

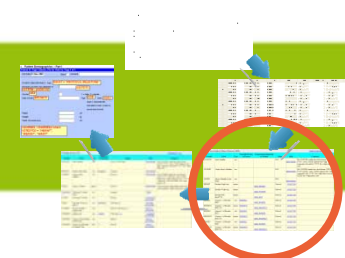
# Traceability SDTM and ADaM



- Analysis Dataset

|    | STUDYID   | USUBJID          | SUBJID | BMI          | BMIGR1       | BMIGR1N | BMIGR2         | BMIGR2N |
|----|-----------|------------------|--------|--------------|--------------|---------|----------------|---------|
| 2  | 9999-0001 | 9999-0001-000001 | 000001 | 27.777777778 | <30 kg/m**2  | 1       | 25-<30 kg/m**2 | 2       |
| 3  | 9999-0001 | 9999-0001-000002 | 000002 | 25.503615702 | <30 kg/m**2  | 1       | 25-<30 kg/m**2 | 2       |
| 4  | 9999-0001 | 9999-0001-000003 | 000003 | 26.175194521 | <30 kg/m**2  | 1       | 25-<30 kg/m**2 | 2       |
| 5  | 9999-0001 | 9999-0001-000004 | 000004 | 35.15625     | >=30 kg/m**2 | 2       | >=30 kg/m**2   | 3       |
| 6  | 9999-0001 | 9999-0001-000005 | 000005 | 30.968858131 | >=30 kg/m**2 | 2       | >=30 kg/m**2   | 3       |
| 7  | 9999-0001 | 9999-0001-000006 | 000006 | 39.697163916 | >=30 kg/m**2 | 2       | >=30 kg/m**2   | 3       |
| 8  | 9999-0001 | 9999-0001-000007 | 000007 | 25.826446281 | <30 kg/m**2  | 1       | 25-<30 kg/m**2 | 2       |
| 9  | 9999-0001 | 9999-0001-000008 | 000008 | 30.103806228 | >=30 kg/m**2 | 2       | >=30 kg/m**2   | 3       |
| 10 | 9999-0001 | 9999-0001-000009 | 000009 | 32.280962683 | >=30 kg/m**2 | 2       | >=30 kg/m**2   | 3       |
| 11 | 9999-0001 | 9999-0001-000010 | 000010 | 28.876133787 | <30 kg/m**2  | 1       | 25-<30 kg/m**2 | 2       |
| 12 | 9999-0001 | 9999-0001-000011 | 000011 | 29.372397383 | <30 kg/m**2  | 1       | 25-<30 kg/m**2 | 2       |
| 13 | 9999-0001 | 9999-0001-000012 | 000012 | 26.714852608 | <30 kg/m**2  | 1       | 25-<30 kg/m**2 | 2       |
| 14 | 9999-0001 | 9999-0001-000013 | 000013 | 32.718619869 | >=30 kg/m**2 | 2       | >=30 kg/m**2   | 3       |
| 15 | 9999-0001 | 9999-0001-000014 | 000014 | 28.719723183 | <30 kg/m**2  | 1       | 25-<30 kg/m**2 | 2       |
| 16 | 9999-0001 | 9999-0001-000015 | 000015 | 32.270420377 | >=30 kg/m**2 | 2       | >=30 kg/m**2   | 3       |

# Traceability SDTM and ADaM



- ADaM define.xml

| Computational Algorithms (ADSL.BMI)    |                                 |                                                                                                                                                                      |                         |                              |         |                          |  |
|----------------------------------------|---------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------|------------------------------|---------|--------------------------|--|
| Reference Name                         |                                 | Computation Method                                                                                                                                                   |                         |                              |         |                          |  |
| ADSL.BMI                               |                                 | Continuous variable, calculated using ADSL.WEIGHT/(ADSL.HEIGHT*0.01)**2 value at visit 3 if visit 3 data not available, the last data collected before randomisation |                         |                              |         |                          |  |
| Computational Algorithms (ADSL.HEIGHT) |                                 |                                                                                                                                                                      |                         |                              |         |                          |  |
| Reference Name                         |                                 | Computation Method                                                                                                                                                   |                         |                              |         |                          |  |
| ADSL.HEIGHT                            |                                 | equal to VS.VSSTRESN when VS.VSTESTCD="HEIGHT"                                                                                                                       |                         |                              |         |                          |  |
| Computational Algorithms (ADSL.WEIGHT) |                                 |                                                                                                                                                                      |                         |                              |         |                          |  |
| Reference Name                         |                                 | Computation Method                                                                                                                                                   |                         |                              |         |                          |  |
| ADSL.WEIGHT                            |                                 | equal to VS.VSSTRESN when VS.VSTESTCD="WEIGHT" and VS.VISITNUM=30 if visit 3 data not available, the last data collected before randomisation                        |                         |                              |         |                          |  |
|                                        |                                 |                                                                                                                                                                      |                         | <a href="#">ADSL.HEIGHT</a>  |         |                          |  |
| WEIGHT                                 | Baseline Weight (kg)            | integer                                                                                                                                                              |                         | <a href="#">ADSL.WEIGHT</a>  | Derived | <a href="#">ANALYSIS</a> |  |
| BMI                                    | Baseline BMI (kg/m**2)          | integer                                                                                                                                                              |                         | <a href="#">ADSL.BMI</a>     | Derived | <a href="#">ANALYSIS</a> |  |
| BMIGR1                                 | Category 1 of Baseline BMI      | text                                                                                                                                                                 | <a href="#">BMIGR1L</a> | <a href="#">ADSL.BMIGR1</a>  | Derived | <a href="#">ANALYSIS</a> |  |
| BMIGR1N                                | Category 1 of Baseline BMI, (N) | integer                                                                                                                                                              | <a href="#">BMIGR1N</a> | <a href="#">ADSL.BMIGR1N</a> | Derived | <a href="#">ANALYSIS</a> |  |
| BMIGR2                                 | Category 2 of Baseline BMI      | text                                                                                                                                                                 | <a href="#">BMIGR2L</a> | <a href="#">ADSL.BMIGR2</a>  | Derived | <a href="#">ANALYSIS</a> |  |
| BMIGR2N                                | Category 2 of Baseline BMI, (N) | integer                                                                                                                                                              | <a href="#">BMIGR2N</a> | <a href="#">ADSL.BMIGR2N</a> | Derived | <a href="#">ANALYSIS</a> |  |
| BMIGR3                                 | Category 3 of Baseline BMI      | text                                                                                                                                                                 | <a href="#">BMIGR3L</a> | <a href="#">ADSL.BMIGR3</a>  | Derived | <a href="#">ANALYSIS</a> |  |
| BMIGR3N                                | Category 3 of Baseline BMI, (N) | integer                                                                                                                                                              | <a href="#">BMIGR3N</a> | <a href="#">ADSL.BMIGR3N</a> | Derived | <a href="#">ANALYSIS</a> |  |

# Traceability SDTM and ADaM

- SDTM define.xml and aCRF

| Value Level Metadata (ValueList.VS.VSTESTCD) |        |                          |      |                        |             |      |         |
|----------------------------------------------|--------|--------------------------|------|------------------------|-------------|------|---------|
| Source Variable                              | Value  | Label                    | Type | Controlled Terminology | Origin      | Role | Comment |
| VSTESTCD                                     | DIABP  | DIASTOLIC BLOOD PRESSURE | text |                        | CRF Page 13 |      |         |
| VSTESTCD                                     | HEIGHT | HEIGHT                   | text |                        | CRF Page 9  |      |         |
| VSTESTCD                                     | PULSE  | PULSE RATE               | text |                        | CRF Page 13 |      |         |
| VSTESTCD                                     | SYSBP  | SYSTOLIC BLOOD PRESSURE  | text |                        | CRF Page 13 |      |         |
| VSTESTCD                                     | WAIST  | WAIST CIRCUMFERENCE      | text |                        | CRF Page 9  |      |         |
| VSTESTCD                                     | WEIGHT | WEIGHT                   | text |                        | CRF Page 9  |      |         |

|          |                                          |                                                                                               |
|----------|------------------------------------------|-----------------------------------------------------------------------------------------------|
| VSSEQ    | Sequence Number                          | patient code                                                                                  |
| VSTESTCD | Vital Signs Test Short Name              | Sequence number (automatically generated) to ensure uniqueness within a dataset for a subject |
| VSTEST   | Vital Signs Test Name                    |                                                                                               |
| VSPOS    | Vital Signs Position of Subject          |                                                                                               |
| VSORRES  | Result or Finding in Original Units      |                                                                                               |
| VSORRESU | Original Units                           |                                                                                               |
| VSSTRESC | Character Result/Finding in Std Format   |                                                                                               |
| VSSTRESN | Numeric Result/Finding in Standard Units |                                                                                               |

**• Patient Demographics – Part I**  
Patient X5 Page 4 (Demo\_V1a for Visit 1a) Page 1 of 1.

Visit Date **11-Dec-2007** Blank ☐ Comment

PATIENT DEMOGRAPHICS - Part I **DSCAT = "PROTOCOL MILESTONE"**

Informed consent was obtained on  **DSSTDTC**

Gender **SEX** ☐ 1 = male, 2 = female

Date of birth **BRTHDTC**  Age **AGE** years **AGEU**

(Age is automatically calculated when screen is saved and closed)

Height  cm

Weight  kg

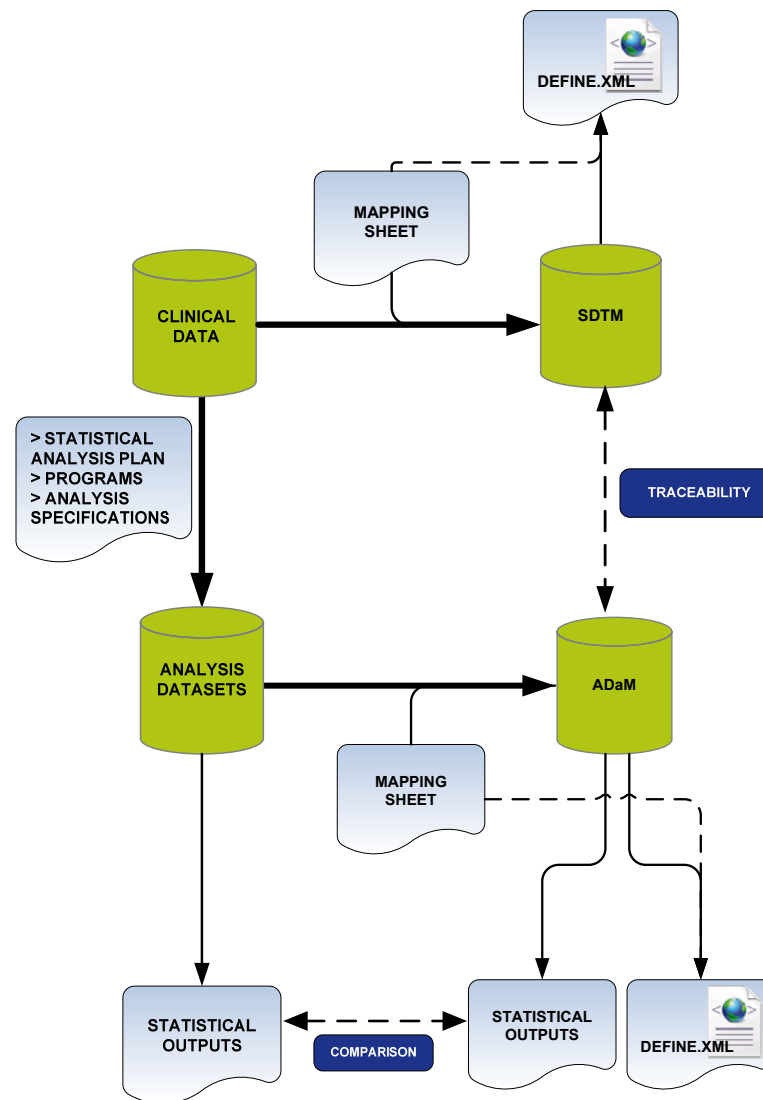
Waist circumference  cm

**VSORRES / VSORRESU where VSTESTCD = "HEIGHT", "WEIGHT", "WAIST"**

# Topics



# ADaM Conversion



# Team Profile and Roles

- **CRO Manager**
  - CDISC expert support
- **Project Manager**  
**Project Manager back-up**
  - Assigned for the duration of the project
  - Single point of contact
- **Mappers**
  - ADaM experts
  - Define mapping
  - Investigate traceability
- **Programmers**
  - Create the conversions programs
  - Perform peer review
- **Data Steward**
  - Maintains the consistency across the project
- **Quality Checker**
  - Perform ADaM datasets review
  - Perform define.xml review



# Conversion Types

- Creation of SDTM variables

## ORIGINAL AD

|   | Trial number | Patient number |
|---|--------------|----------------|
| 1 | 9999-0001    | 1              |
| 2 | 9999-0001    | 1              |
| 3 | 9999-0001    | 1              |
| 4 | 9999-0001    | 2              |
| 5 | 9999-0001    | 2              |
| 6 | 9999-0001    | 2              |
| 7 | 9999-0001    | 3              |
| 8 | 9999-0001    | 3              |
| 9 | 9999-0001    | 3              |

## ADaM AD

|   | Study Identifier | Unique Subject Identifier | Subject Identifier for the Study |
|---|------------------|---------------------------|----------------------------------|
| 1 | 9999-0001        | 9999-0001-000001          | 000001                           |
| 2 | 9999-0001        | 9999-0001-000002          | 000002                           |
| 3 | 9999-0001        | 9999-0001-000003          | 000003                           |

# Conversion Types

- Minor conversion
  - Contents unchanged, metadata changes

## ORIGINAL AD

|   | STUDY     | PTNO | BAGE | BAGEC1 | BAGECDC1    | BAGEC2 | BAGECDC2     |
|---|-----------|------|------|--------|-------------|--------|--------------|
| 1 | 9999-0001 | 1    | 74   | 2      | 65-74 years | 4      | 65-<75 years |
| 2 | 9999-0001 | 2    | 46   | 1      | <65 years   | 2      | 45-<55 years |
| 3 | 9999-0001 | 3    | 60   | 1      | <65 years   | 3      | 55-<65 years |

## ADaM AD

|   | STUDYID   | USUBJID          | SUBJID | AGE      | AGEU | AGEGR1      | AGEGR1N | AGEGR2       | AGEGR2N |
|---|-----------|------------------|--------|----------|------|-------------|---------|--------------|---------|
| 1 | 9999-0001 | 9999-0001-000001 | 000001 | 74 YEARS |      | 65-74 years | 2       | 65-<75 years | 4       |
| 2 | 9999-0001 | 9999-0001-000002 | 000002 | 46 YEARS |      | <65 years   | 1       | 45-<55 years | 2       |
| 3 | 9999-0001 | 9999-0001-000003 | 000003 | 60 YEARS |      | <65 years   | 1       | 55-<65 years | 3       |

# Conversion Types

- Format values
  - Content and metadata changes

## ORIGINAL AD

|   | STUDY     | PTNO | SEX | SEXDC  |
|---|-----------|------|-----|--------|
| 1 | 9999-0001 | 1    | 1   | Male   |
| 2 | 9999-0001 | 2    | 2   | Female |
| 3 | 9999-0001 | 3    | 1   | Male   |

## ADaM AD

|   | STUDYID   | USUBJID          | SUBJID | SEX | SEXN | SEXDC  |
|---|-----------|------------------|--------|-----|------|--------|
| 1 | 9999-0001 | 9999-0001-000001 | 000001 | M   | 1    | Male   |
| 2 | 9999-0001 | 9999-0001-000002 | 000002 | F   | 2    | Female |
| 3 | 9999-0001 | 9999-0001-000003 | 000003 | M   | 1    | Male   |

# Conversion Types

- Transpose
  - Observations become variables
  - Variables become observations

## ORIGINAL AD

|   | Trial number | Patient number | Analysis set | Analysis set decode | Included in analysis set | Included in analysis set decode |
|---|--------------|----------------|--------------|---------------------|--------------------------|---------------------------------|
| 1 | 9999-0001    | 1              | FAS          | Full analysis set   | 0                        | No                              |
| 2 | 9999-0001    | 1              | PPS          | Per protocol set    | 0                        | No                              |
| 3 | 9999-0001    | 1              | RS           | Randomised set      | 0                        | No                              |
| 4 | 9999-0001    | 2              | FAS          | Full analysis set   | 1                        | Yes                             |
| 5 | 9999-0001    | 2              | PPS          | Per protocol set    | 0                        | No                              |
| 6 | 9999-0001    | 2              | RS           | Randomised set      | 1                        | Yes                             |
| 7 | 9999-0001    | 3              | FAS          | Full analysis set   | 1                        | Yes                             |
| 8 | 9999-0001    | 3              | PPS          | Per protocol set    | 1                        | Yes                             |
| 9 | 9999-0001    | 3              | RS           | Randomised set      | 1                        | Yes                             |

## ADaM AD

|   | Study Identifier | Unique Subject Identifier | Subject Identifier for the Study | Full Analysis Set Population Flag | Full Analysis Set Population Flag, (N) | Per-Protocol Population Flag | Per-Protocol Population Flag, (N) | Randomized Population Flag | Randomized Population Flag, (N) |
|---|------------------|---------------------------|----------------------------------|-----------------------------------|----------------------------------------|------------------------------|-----------------------------------|----------------------------|---------------------------------|
| 1 | 9999-0001        | 9999-0001-000001          | 000001                           | N                                 | 0                                      | N                            | 0                                 | N                          | 0                               |
| 2 | 9999-0001        | 9999-0001-000002          | 000002                           | Y                                 | 1                                      | N                            | 0                                 | Y                          | 1                               |
| 3 | 9999-0001        | 9999-0001-000003          | 000003                           | Y                                 | 1                                      | Y                            | 1                                 | Y                          | 1                               |

# Traceability

- Variables originating from SDTM
  - SDTM variables are retained in ADaM ADs for traceability
  - SDTM variables are unchanged
    - same name, same type, same label (metadata)
    - and same content (data)
- Derived variables
  - Original computational algorithm for derived AD variable(s) based on original clinical database
  - New computational algorithm needs to be based on SDTM database
  - New computational algorithm is included into ADaM define.xml

# Topics



# Quality Control

- **QC is partially automated**
  - Electronic QC (CDISC Compliance Checks – SDTM&ADAM)
  - Manual QC
  - QC on Consistency (Data Steward)
- **QC on:**
  - Mapping
  - ADaM Datasets
  - Define.xml
- **QC is supported by documentation**
- **For each study a Data Handling Report is generated**

## QC Tier 1: CDISC Compliance Checks

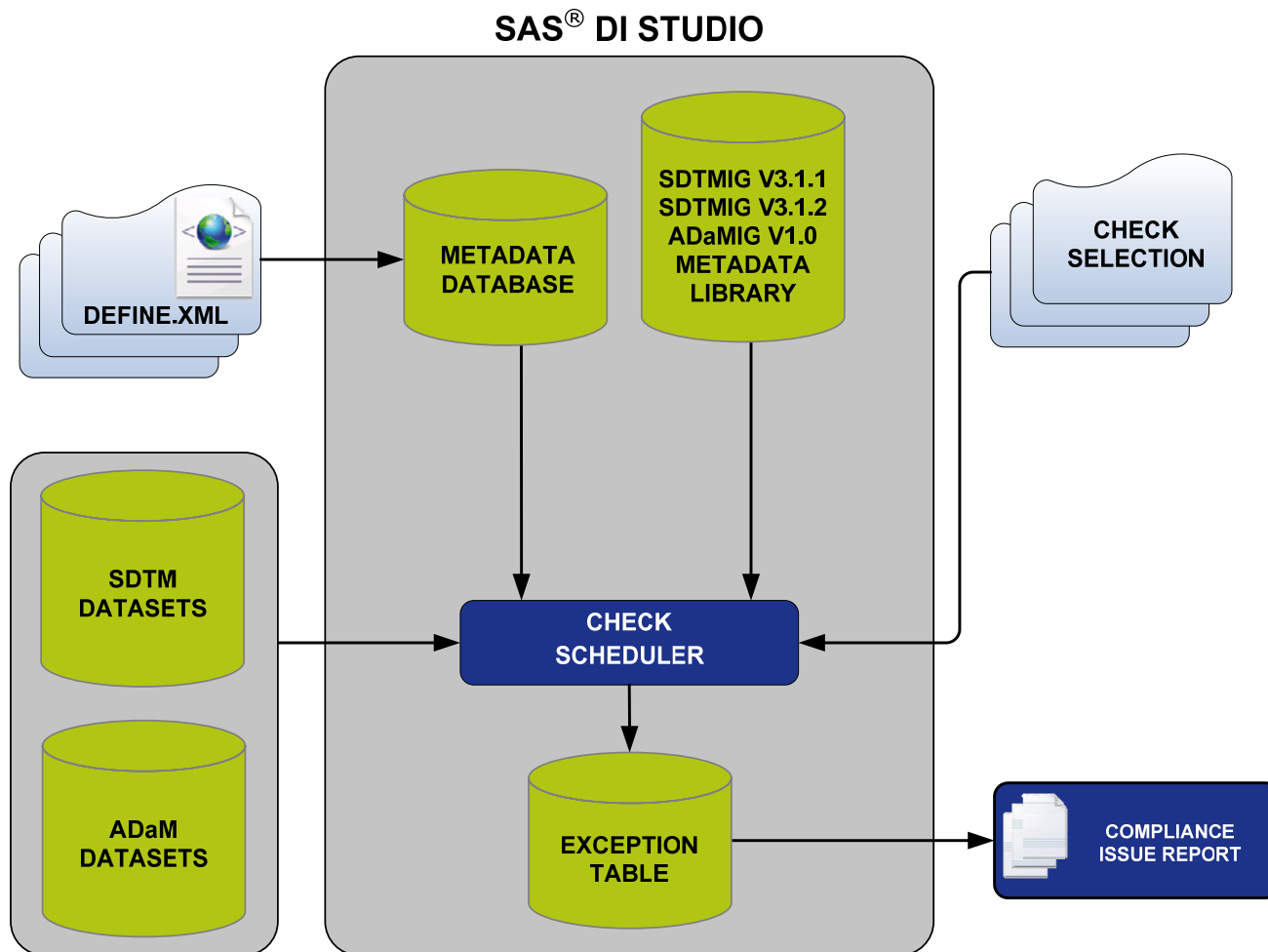
**We have created an expanded & enhanced list of checks**

- 154 WebSDM <sup>TM</sup> checks
- Total check package:

|                               | SDTMIG<br>V3.1.1 | SDTMIG<br>V3.1.2 | ADaMIG<br>V1.0 |
|-------------------------------|------------------|------------------|----------------|
| Data checks                   | 141              | 219              | 45             |
| Metadata checks               | 68               | 117              | 51             |
| Mapping checks                | 56               | 57               | 12             |
| Project consistency<br>checks | 20               | 20               | 20             |

**CDISC compliance checks list is growing continuously**

## QC Tier 1: Application Flowchart



## QC Tier 2: Manual QC

- **100% manual QC on a random sample**
- **Supported by checklists**
- **Supported by a QC content tool on source and target**

### DATA.ADSL

Created: 08APR10:08:52:02  
# obs : 503  
Keys :

| #  | Variable | Label                            | Type | Length | Contents                                                                                                    |
|----|----------|----------------------------------|------|--------|-------------------------------------------------------------------------------------------------------------|
| 1  | STUDYID  | Study Identifier                 | CHAR | 200    | + 1 distinct values, 0 missing values, all shown                                                            |
| 2  | USUBJID  | Unique Subject Identifier        | CHAR | 200    | + 503 distinct values, 0 missing values, all shown                                                          |
| 3  | SUBJID   | Subject Identifier for the Study | CHAR | 200    | + 503 distinct values, 0 missing values, all shown                                                          |
| 4  | SITEID   | Study Site Identifier            | CHAR | 200    | + 63 distinct values, 0 missing values, all shown                                                           |
| 5  | PTNOTYP  | Type of trial participant        | CHAR | 200    | + 1 distinct values, 0 missing values, all shown                                                            |
| 6  | INVTNAM  | Investigator Name                | CHAR | 200    | + 62 distinct values, 0 missing values, all shown                                                           |
| 7  | COUNTRY  | Country                          | CHAR | 200    | + 11 distinct values, 0 missing values, all shown                                                           |
| 8  | COUNTRDC | Country, Decode                  | CHAR | 40     | + 11 distinct values, 0 missing values, all shown                                                           |
| 9  | REGION   | Region                           | CHAR | 40     | + 2 distinct values, 0 missing values, all shown                                                            |
| 10 | AGE      | Age                              | NUM  | 8      | + 52 distinct values, 0 missing values, all shown<br>Mean: 55.708 Minimum: 24 Maximum: 74 Missing values: 0 |
| 11 | AGEU     | Age Units                        | CHAR | 200    | + 1 distinct values, 0 missing values, all shown                                                            |
| 12 | AGEGR1   | Age Group 1                      | CHAR | 20     | + 3 distinct values, 0 missing values, all shown                                                            |
| 13 | AGEGR1N  | Age Group 1, (N)                 | NUM  | 8      | + 3 distinct values, 0 missing values, all shown<br>Mean: 1.225 Minimum: 1 Maximum: 3 Missing values: 0     |
| 14 | AGEGR2   | Age Group 2                      | CHAR | 20     | + 5 distinct values, 0 missing values, all shown                                                            |
| 15 | AGEGR2N  | Age Group 2, (N)                 | NUM  | 8      | + 5 distinct values, 0 missing values, all shown<br>Mean: 2.646 Minimum: 1 Maximum: 5 Missing values: 0     |
| 16 | AGEGR3   | Age Group 3                      | CHAR | 20     | + 2 distinct values, 0 missing values, all shown                                                            |
| 17 | AGEGR3N  | Age Group 3, (N)                 | NUM  | 8      | + 2 distinct values, 0 missing values, all shown                                                            |

11 distinct values, 0 missing values, all shown

|             |        |
|-------------|--------|
| Croatia     | (17x)  |
| India       | (135x) |
| Israel      | (21x)  |
| Italy       | (15x)  |
| Malaysia    | (72x)  |
| Netherlands | (33x)  |
| Poland      | (11x)  |
| Romania     | (24x)  |
| Slovakia    | (62x)  |
| Thailand    | (24x)  |
| Ukraine     | (89x)  |

3 distinct values, 0 missing values, all shown

|             |        |
|-------------|--------|
| 65-74 years | (97x)  |
| <65 years   | (398x) |
| >=75 years  | (8x)   |

# QC Tier 3: Data Steward

- **Maintains consistency of metadata across project**
- **Uses the metadata repository**
- **Electronic consistency checks**

## Table of Contents

1. DATASET
2. DATASET DESCRIPTION
3. DATASET CLASS
4. DATASET STRUCTURE
5. DATASET PURPOSE
6. DATASET SORTING KEYS

## VARIABLE LABEL

| DOMAIN | VARIABLE | VARIABLE LABEL                         | S1218_0005 | S1218_0006 | S1218_0017 | GLBSTND |
|--------|----------|----------------------------------------|------------|------------|------------|---------|
| ADSL   | FASCOFN  | FAS Completers Population Flag, (N)    | X          | X          |            | .       |
| ADSL   | FASCOFN  | FAS Completers Population Flag, Num    |            |            | X          | .       |
| ADSL   | FASFN    | Full Analysis Set Population Flag, (N) | X          | X          |            | .       |
| ADSL   | FASFN    | Full Analysis Set Population Flag, Num |            |            | X          | .       |
| ADSL   | FASMTTFN | FAS MTT Population Flag, (N)           | X          | X          |            | .       |
| ADSL   | FASMTTFN | FAS MTT Population Flag, Num           |            |            | X          | .       |
| ADSL   | PPROTFN  | Per-Protocol Population Flag, (N)      | X          | X          |            | .       |
| ADSL   | PPROTFN  | Per-Protocol Population Flag, Num      |            |            | X          | .       |
| ADSL   | RACEGR1  | Pooled Race Group 1                    |            |            | X          | .       |
| ADSL   | RACEGR1N | Pooled Race Group 1 (N)                |            |            | X          | .       |
| ADSL   | RANDFN   | Randomized Population Flag, (N)        | X          | X          |            | .       |

# Communication Topics

- Report Source Data Issues
  - Empty variables
  - Exclusion of screen failures
  - Unclear computational algorithms
  - Traceability issues with SDTM
- Sponsor Feedback
  - Clarifications computational algorithms
  - QC comments

# Topics



# Challenges

- Understanding original analysis datasets and computational algorithms
  - Understanding derived variables in original ADs
- This type of project is always on critical path for a submission
  - Short timelines
  - Large team

# Conclusion

- We now understand better how FDA feels
- SDTM is the basis for analysis and therefore needs to be complete
- Results in the clinical study report must be reproducible by FDA reviewers from the newly created ADaM analysis datasets
- Traceability most difficult part in ADaM conversion
- In an ideal world, analysis datasets are created from SDTM datasets, thereby ensuring 100% traceability



**Thank you  
for your attention**

**Florence Somers**

Practice Manager  
Statistical Programming  
Business & Decision Life Sciences -  
Brussels

Tel +32 2 774 11 00  
Fax +32 2 774 11 99  
Mobile +32 491 15 37 47  
[florence.somers@businessdecision.com](mailto:florence.somers@businessdecision.com)

**Andrew Winkler**

Sr. Principal, R&D  
Business & Decision Life Sciences -  
North America

Tel +1 919-428-3592  
[andrew.winkler@businessdecision.com](mailto:andrew.winkler@businessdecision.com)

[www.businessdecision-lifesciences.com](http://www.businessdecision-lifesciences.com)



**DRIVE YOUR PERFORMANCE**