

Update @ SAS

[SAS 9.4, STAT, Toolkit, CDI, and JMP® Clinical]

PhUSE SDE, Copenhagen, 28 May 2013

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Content

- **SAS 9.4** /June
- **SAS Stat v12.3** /June
- **Clinical Standards Toolkit v1.5** /May
- **Clinical Data Integration v2.4** /July
- **JMP Clinical v4.1** /July

SAS 9.4

SAS 9.4 - Highlights

Platform and Foundation

- **New Languages**
 - DS2 Language
 - FedSQL Language
- **Enhanced Output**
 - ODS
 - PowerPoint
- **Increased Security**
- **JSON**
- **Cloud Enablement**
- **HP Enablement**

SAS STAT v12.3

What's new?

SAS/STAT®

- PROC HPLOGISTIC
- PROC HPREG
- PROC HPLMIXED
- PROC HPNLMOD
- **PROC HPSPLIT**
- **PROC HPGENSELECT**

Common set

- HPDS2
- HPDMDB
- HPSAMPLE
- HPSUMMARY
- HPIMPUTE
- HPBIN
- HPCORR

New procedures

HPSPPLIT and HPGENSELECT

- **HPSPPLIT**
 - Build decision trees where optimal splits are calculated using either entropy, fastCHAID (experimental) or Gini
 - Creates scoring code and rules file
- **HPGENSELECT**
 - performs model selection for generalized linear models (GLMs), Poisson regression, negative binomial regression etc.
 - provides forward, backward and stepwise regression and AIC, SBC and AICC selection criteria
 - LASSO-type methods and graphics coming up ...

```
proc hpgenselect data=getStarted;
  class C1-C5;
  model Y = C1-C5 / Distribution=Poisson Link=Log;
run;
```

The HPGENSELECT Procedure Performance Information

Execution Mode	Single-Machine
Number of Threads	4

Fit Statistics

-2 Log Likelihood	290.16169
AIC (smaller is better)	322.16169
AICC (smaller is better)	328.71590
BIC (smaller is better)	363.84441
Pearson Chi-Square	77.76937
Pearson Chi-Square/DF	0.92583

What is SAS® high-performance Analytics?

- Take advantage of all cores available on the Symmetric Multi-Processing (SMP) system using multi-threading
- Algorithms used are suited for large data and/or shorter run time
- Not all algorithms used in HP-proc's are the same as used in the regular proc (e.g. results using PROC LOGISTIC might differ from the results from PROC HPLOGISTIC)
- Some proc's are already multi-threaded (e.g. PROC REG)
- Use “all” the data (vs. “sample” data), employ complex modeling techniques, and perform frequent model iterations to get more accurate insights

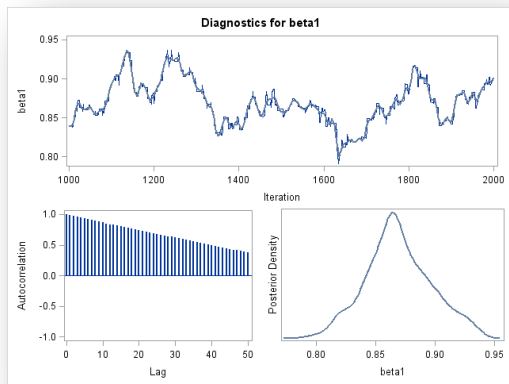
Why SAS® High-performance proc's?

- Benefits

- HP PROC's included in current licenses
- Meet current analytical demands, but also provide a path to meet future growth requirements
- Flexibility for users to move to an distributed, in-memory processing architecture with reduced pricing
- Derive insights with speed for high-value and time-sensitive decisions
- Help to modernize customer's analytical programs and leverage existing multicore servers (i.e. without new investments in many cases) for faster processing

Bayesian analysis using proc mcmc (1/2)

Example

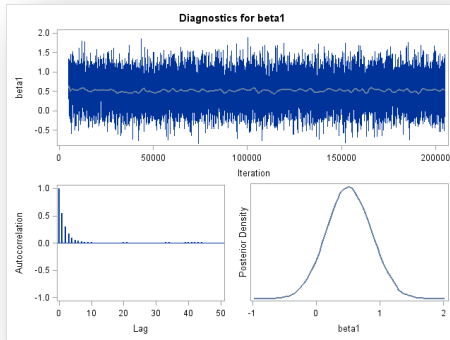


- `proc mcmc data=sasuser.birth diag=all dic plots(smooth)=all seed=27513;`
- `parms (beta0 beta1 beta2 beta3 beta4) 0;`
- `prior beta: ~ normal(0, var=100);`
- `p = logistic(beta0 + beta1*alcohol + beta2*hist_hyp + beta3*mother_wt + beta4*prev_pretrm);`
- `model low ~ binary(p);`
- `run;`

Posterior Summaries						
Parameter	N	Mean	Standard Deviation	Percentiles		
				25%	50%	75%
beta0	1000	-0.5015	0.1145	-0.6206	-0.4946	-0.4174
beta1	1000	0.8697	0.0275	0.8515	0.8671	0.8864
beta2	1000	0.2190	0.0461	0.1986	0.2283	0.2483
beta3	1000	-0.00695	0.00152	-0.00793	-0.00688	-0.00585
beta4	1000	0.9999	0.0300	0.9791	0.9989	1.0196

Bayesian analysis using proc mcmc (2/2)

Example



- ```
proc mcmc data=sasuser.birth outpost=birthout
 diag=all dic propcov=quanew nbi=5000 ntu=5000
 nmc=200000 thin=5 mchistory=brief
 plots(smooth)=all seed=27513;

 parms (beta0 beta1 beta2 beta3 beta4) 0;

 prior beta: ~ normal(0, var=100);

 p = logistic(beta0 + beta1*alcohol +
 beta2*hist_hyp +beta3*mother_wt +
 beta4*prev_pretrm);

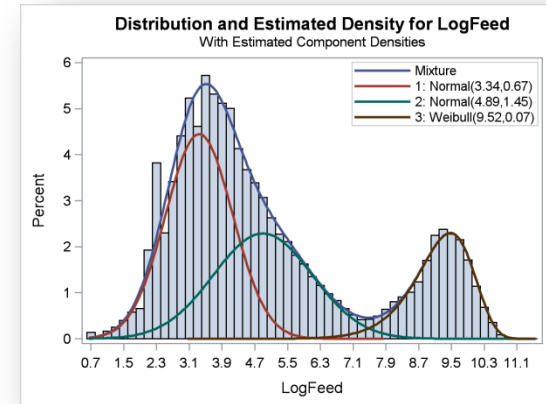
 model low ~ binary(p);

run;
```

| Posterior Summaries |       |         |                    |             |         |         |
|---------------------|-------|---------|--------------------|-------------|---------|---------|
| Parameter           | N     | Mean    | Standard Deviation | Percentiles |         |         |
|                     |       |         |                    | 25%         | 50%     | 75%     |
| beta0               | 40000 | 0.8946  | 0.8837             | 0.2886      | 0.8821  | 1.4834  |
| beta1               | 40000 | 0.5164  | 0.3519             | 0.2787      | 0.5141  | 0.7539  |
| beta2               | 40000 | 1.9277  | 0.7360             | 1.4250      | 1.9049  | 2.4143  |
| beta3               | 40000 | -0.0181 | 0.00690            | -0.0226     | -0.0179 | -0.0133 |
| beta4               | 40000 | 1.3310  | 0.4460             | 1.0309      | 1.3255  | 1.6246  |

# Future focus areas and statistical trends

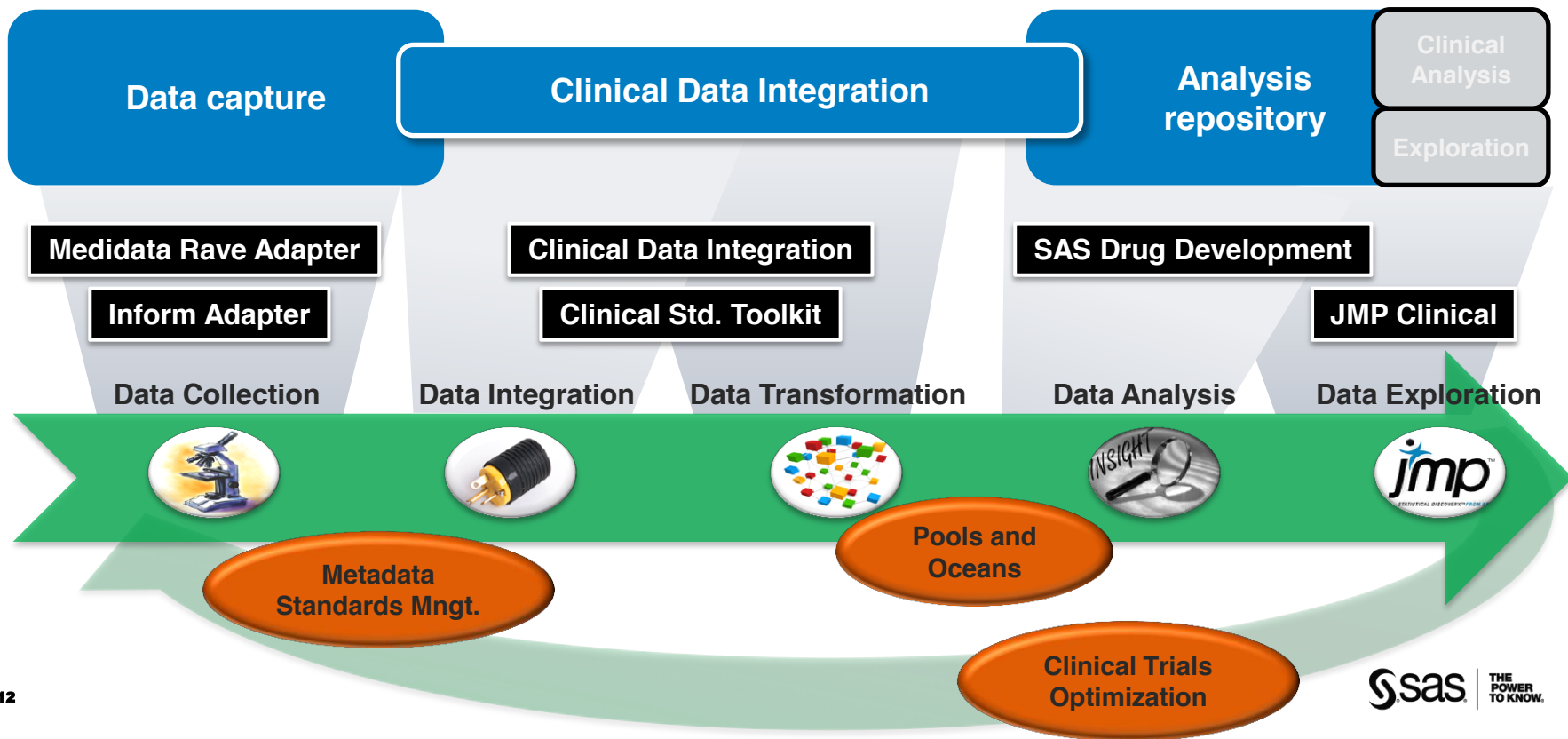
- Quantile modeling
  - e.g. PROC QUANTREG and PROC QUANTSELECT
- Bayesian analysis
  - Enhanced functionality including BAYES in PROC FMM
- Postfitting inference
  - Including hypothesis testing and scoring
- Missing data analysis
  - PROC MI and PROC MIANALYZE
- Finite mixture models
- Specialized survival analysis
- Structural equation modeling



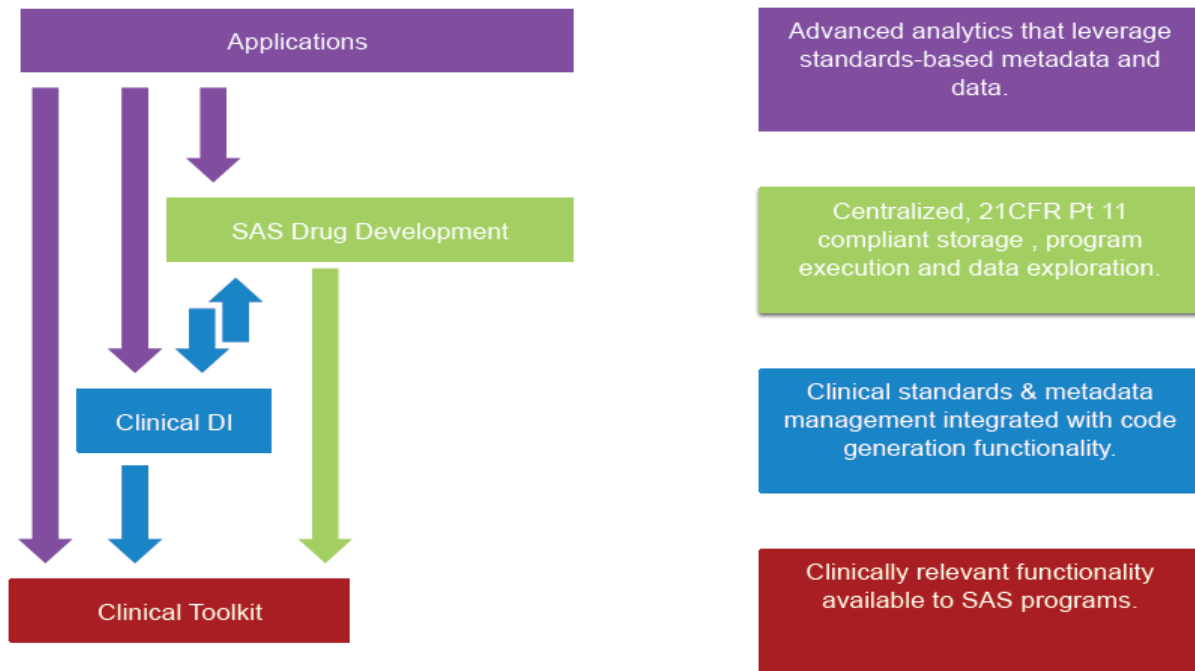
# Content

- **SAS 9.4** /June
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# SAS supporting Drug Development



# Relationship between solutions



# Clinical Standards Toolkit

## – what is it?

- A collection of “tools”, providing an initial set of standards and functionality
  - Macros
  - Metadata (Datasets defining data structures)
  - Sample driver programs
  - Full samples (examples)
- Focused on standards as defined by CDISC (but not limited to CDISC)
- Evolving and growing with updates and releases (twice yearly)
- Available to all SAS users as open source SAS Macros
  - Designed as an integral part of Clinical Data Integration (CDI)



# Clinical Standards Toolkit

## – new key features in v1.5

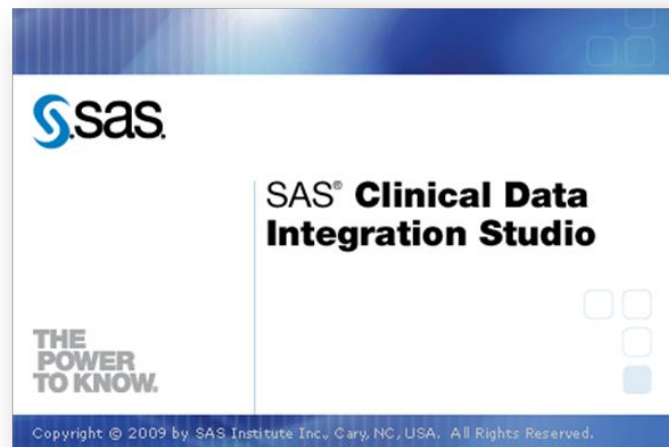
- SDTM 3.1.3 (includes 3.1.1 and 3.1.2) \*
- SEND 3.0 data structures only, no checks included \*
- ADaM 2.1 with any additional data structures including ADAE \*
- Define.pdf generation \*
- Easily update new NCI CT versions
- ODM 1.3 and 1.3.1
- ODM form data into SAS data set
- Value-level metadata into define.xml
- Compatible with SDD 4.x
- Internationalization - multi-byte, UTF8 character SAS data support

# **SAS® Clinical Data Integration**

## **– what is it?**

A data transformation solution designed to:

- Integrate, aggregate and map data
- Standardize data to CDISC data standards
- Extend data standards to create and manage sponsor customized standards (e.g. SDTM+)
- Govern & manage data standards and controlled terminology
- Conduct quality (compliance) checks of data against standards
- Easy creation of define.xml
- Automating the collection and management of metadata



# **SAS® Clinical Data Integration**

## **– new key features in v2.4**

- SDTM 3.1.3 (includes 3.1.1 and 3.1.2)
- ADaM 2.1
- Bulk manipulation of properties defining data standards
  - Domain properties, Column properties – both study level and global standards level
- Import of define.xml to define study, data structures, controlled terminology
- Use clinical objects within Clinical Data Integration change control
- Choice of Study/Submission templates (different folder structures)
- Internationalization - multi-byte, UTF8 character SAS data support
- SMB pricing

# JMP Clinical – what is it?

A statistical & graphical tool helping companies to:

- **Analyze & visualize**
- **Explore patterns**
- **Enhance safety & efficacy assessments**

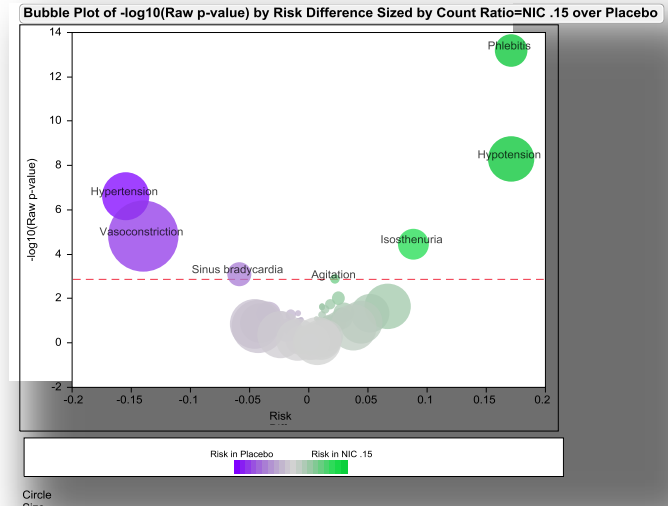
...of CDISC-standardized clinical data



# JMP Clinical

## – new key features in v4.1

- Delta review (Snapshot comparison) - view different snapshots of clinical trial data
  - Including Domain viewer
- Integrate and perform JMP Clinical analysis directly on a SAS Metadata server
- Industry standard tabulated views to many visualizations (interactive)
- Improved visualizations
- Data quality and fraud detection
- Clinical trial Bayesian signal detection



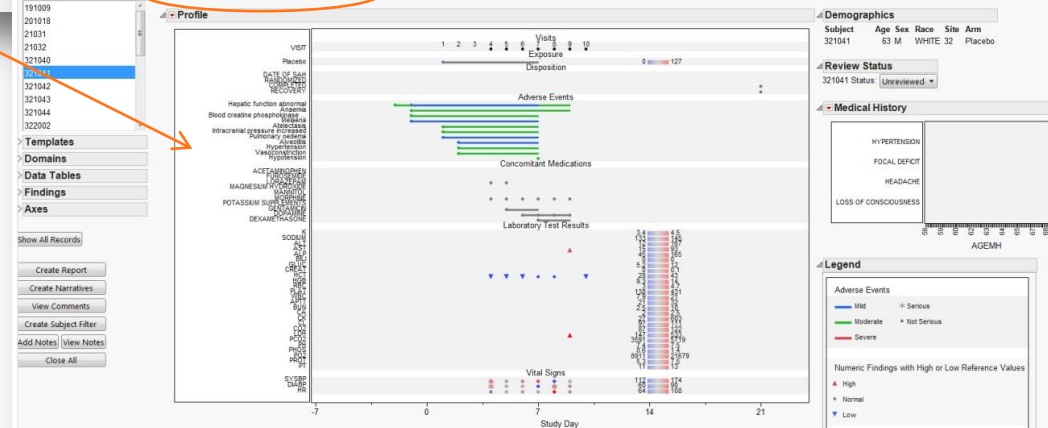
# Delta Review

- Swap patient profile view between:

- Show all records
- Show new or modified records



Displaying records that are New, Modified or Non-Urgent



# Domain Viewer

- Provide quick overview if domain data value is:

- New (yellow)
- Modified (red)
- Stable (green)
- Non-unique (black)
- Dropped (blue)

- Support data review process

## Output Description

### Domains

AE

### Drill Downs

Select a Domain Above then Click

View Domain

View Domain Notes

Show Dropped Records

Show Duplicates

Show Domain Keys

Select Records then Click

Profile Subjects

Create Subject Filter

Add Record-Level Notes

View Record-Level Notes

## Domain Viewer

Codes for record-level review flags (merging based on domain keys):

NEW: Record was not previously available.

MODIFIED: Record was previously available, but data in one or more variables has changed.

STABLE: Record was previously available, no data has changed.

NON-UNIQUE: Record was previously available, but duplicates exist in the prior or current snapshot so that comparisons are not possible due to non-uniqueness of records.

DROPPED: Record was previously available, but does not exist current snapshot. Click 'Show Dropped Records' to view records not in the selected domain, if available.

Note: NEW records may include duplicates not considered among the records labeled NON-UNIQUE. Click 'Show Duplicates' to view records not in the selected domain, if available.

Note: All data is subset to the selected population and filtered subjects from the dialog.

| Study Identifier | Domain Abbreviation | Unique Subject Identifier | Subject Identifier for the Study | Subject Reference Start Date/Time | Subject Reference End Date/Time | Study Site Identifier | Investigator Identifier | Investigator Name | Date/Time of Birth | Age      | Age Units | Sex |
|------------------|---------------------|---------------------------|----------------------------------|-----------------------------------|---------------------------------|-----------------------|-------------------------|-------------------|--------------------|----------|-----------|-----|
| 567 NICA5AH1     | DM                  | 321023                    | 321023                           | 1989-02-26T09:00:00               | 1989-02-06T09:00:00             | 32                    | 1A                      | 321A              | 1929-02-12         | 59 YEARS | M         | Wh  |
| 568 NICA5AH1     | DM                  | 321024                    | 321024                           | 1989-02-08T08:00:00               | 1989-02-17T10:00:00             | 32                    | 1A                      | 321A              | 1912-06-11         | 76 YEARS | F         | Wh  |
| 569 NICA5AH1     | DM                  | 321025                    | 321025                           | 1989-02-22T08:00:00               | 1989-02-27T15:30:00             | 32                    | 1F                      | 321F              | 1926-02-15         | 63 YEARS | F         | Wh  |
| 570 NICA5AH1     | DM                  | 321026                    | 321026                           | 1989-03-14T07:00:00               | 1989-03-25T08:00:00             | 32                    | 1A                      | 321A              | 1930-07-31         | 58 YEARS | F         | Wh  |
| 571 NICA5AH1     | DM                  | 321027                    | 321027                           | 1989-04-04T14:15:00               | 1989-04-16T18:00:00             | 32                    | 1F                      | 321F              | 1958-10-20         | 30 YEARS | F         | Wh  |
| 572 NICA5AH1     | DM                  | 321029                    | 321029                           | 1989-04-14T09:30:00               | 1989-04-25T09:00:00             | 32                    | 1A                      | 321A              | 1945-10-14         | 43 YEARS | F         | Wh  |
| 573 NICA5AH1     | DM                  | 321030                    | 321030                           | 1989-05-02T12:15:00               | 1989-05-13T11:45:00             | 32                    | 1A                      | 321A              | 1949-02-17         | 40 YEARS | F         | Wh  |
| 574 NICA5AH1     | DM                  | 321031                    | 321031                           | 1989-05-05T16:30:00               | 1989-05-17T06:00:00             | 32                    | 1A                      | 321A              | 1917-09-28         | 71 YEARS | F         | Wh  |
| 575 NICA5AH1     | DM                  | 321032                    | 321032                           | 1989-05-08T14:45:00               | 1989-05-20T09:00:00             | 32                    | 1A                      | 321A              | 1939-12-02         | 49 YEARS | M         | Wh  |
| 576 NICA5AH1     | DM                  | 321033                    | 321033                           | 1989-05-13T17:45:00               | 1989-05-25T08:00:00             | 32                    | 1F                      | 321F              | 1946-07-20         | 42 YEARS | F         | Wh  |
| 577 NICA5AH1     | DM                  | 321034                    | 321034                           | 1989-05-17T06:45:00               | 1989-05-29T09:30:00             | 32                    | 1A                      | 321A              | 1940-09-13         | 48 YEARS | F         | Wh  |
| 578 NICA5AH1     | DM                  | 321035                    | 321035                           | 1989-06-12T14:45:00               | 1989-06-23T09:00:00             | 32                    | 1A                      | 321A              | 1935-07-08         | 53 YEARS | M         | Wh  |
| 579 NICA5AH1     | DM                  | 321036                    | 321036                           | 1989-06-16T07:10:00               | 1989-06-17T13:00:00             | 32                    | 1F                      | 321F              | 1932-07-07         | 56 YEARS | F         | OT  |
| 580 NICA5AH1     | DM                  | 321037                    | 321037                           | 1989-06-19T15:00:00               | 1989-06-30T06:00:00             | 32                    | 13                      | 3213              | 1936-11-15         | 52 YEARS | F         | Wh  |
| 581 NICA5AH1     | DM                  | 321038                    | 321038                           | 1989-06-30T07:45:00               | 1989-07-11T08:00:00             | 32                    | 13                      | 3213              | 1921-11-02         | 67 YEARS | F         | Wh  |
| 582 NICA5AH1     | DM                  | 321039                    | 321039                           | 1989-07-06T07:45:00               | 1989-07-14T17:30:00             | 32                    | 1F                      | 321F              | 1922-05-12         | 67 YEARS | F         | Wh  |
| 583 NICA5AH1     | DM                  | 321040                    | 321040                           | 1989-07-22T12:25:00               | 1989-08-02T09:00:00             | 32                    | 1A                      | 321A              | 1959-01-03         | 30 YEARS | M         | OT  |
| 584 NICA5AH1     | DM                  | 321041                    | 321041                           | 1989-07-29T11:15:00               | 1989-08-04T12:30:00             | 32                    | 1A                      | 321A              | 1926-04-27         | 63 YEARS | M         | Wh  |
| 585 NICA5AH1     | DM                  | 321042                    | 321042                           | 1989-07-31T10:45:00               | 1989-08-12T16:00:00             | 32                    | 13                      | 3213              | 1947-12-10         | 41 YEARS | M         | BL  |
| 586 NICA5AH1     | DM                  | 321043                    | 321043                           | 1989-08-07T15:30:00               | 1989-08-25T10:00:00             | 32                    | 1F                      | 321F              | 1929-07-26         | 60 YEARS | M         | Wh  |
| 587 NICA5AH1     | DM                  | 321044                    | 321044                           | 1989-08-07T12:15:00               | 1989-08-16T10:15:00             | 32                    | 1A                      | 321A              | 1940-03-08         | 49 YEARS | M         | OT  |
| 588 NICA5AH1     | DM                  | 322001                    | 322001                           | 1989-04-21T21:00:00               | 1989-05-03T19:00:00             | 32                    | 2A                      | 322A              | 1913-10-13         | 75 YEARS | F         | Wh  |
| 589 NICA5AH1     | DM                  | 322002                    | 322002                           | 1989-08-03T09:00:00               | 1989-08-14T14:00:00             | 32                    | 2A                      | 322A              | 1932-06-21         | 57 YEARS | F         | Wh  |
| 590 NICA5AH1     | DM                  | 331001                    | 331001                           | 1988-06-19T07:45:00               | 1988-07-01T14:00:00             | 33                    | 1A                      | 331A              | 1958-02-25         | 30 YEARS | M         | BL  |
| 591 NICA5AH1     | DM                  | 331002                    | 331002                           | 1988-07-09T16:30:00               | 1988-07-17T17:00:00             | 33                    | 1A                      | 331A              | 1946-12-27         | 41 YEARS | F         | Wh  |
| 592 NICA5AH1     | DM                  | 331003                    | 331003                           | 1988-10-11T17:30:00               | 1988-10-15T13:55:00             | 33                    | 1A                      | 331A              | 1921-11-01         | 66 YEARS | F         | Wh  |
| 593 NICA5AH1     | DM                  | 331004                    | 331004                           | 1988-10-14T20:10:00               | 1988-10-25T01:00:00             | 33                    | 1E                      | 331E              | 1948-06-02         | 40 YEARS | F         | BL  |

| Study Name                   | Keys            | Keys Values of notes | Domain | Analytical Process | User         | Note                                                                                           | Date of Note         |
|------------------------------|-----------------|----------------------|--------|--------------------|--------------|------------------------------------------------------------------------------------------------|----------------------|
| 1 Nicardipine Early Snapshot | STUDYID USUBJID | NICA5AH1-321040      | DM     | ManageStudies      | JMP Clinical | Value change in Subject Reference End Date/Time (RFENDTC) from Missing to 1989-08-02T09:00:00. | 25Apr2013 4:33:21 PM |
| 2 Nicardipine Early Snapshot | STUDYID USUBJID | NICA5AH1-321041      | DM     | ManageStudies      | JMP Clinical | Value change in Subject Reference End Date/Time (RFENDTC) from Missing to 1989-08-04T12:30:00. | 25Apr2013 4:33:21 PM |
| 3 Nicardipine Early Snapshot | STUDYID USUBJID | NICA5AH1-321042      | DM     | ManageStudies      | JMP Clinical | Value change in Subject Reference End Date/Time (RFENDTC) from Missing to 1989-08-12T16:00:00. | 25Apr2013 4:33:21 PM |

## Relevant links

### **Statistical papers**

<http://support.sas.com/rnd/app/stat/papers/index.html>

### **SAS Analytics Network (in Danish)**

<http://www.sas.com/reg/offer/dk/sas-analytics-network>

### **More SAS/STAT news**

<http://www.sas.com/technologies/analytics/statistics/stat/>

### **More on SAS Clinical Data Integration:**

<http://www.sas.com/industry/pharma/cdi/#section=1>

### **More on JMP Clinical:**

<http://www.jmp.com/software/clinical/>

