



Science For A Better Life

AirTracer

Lighten up clinical trials



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Agenda

- Who is interested in lighten up clinical trials?
- What information should be available?
- How to collect these information?
- When will these information be used?
- Where can it be displayed?





Motivation



Number of subjects with protocol deviations by category and type (Safety analysis set)

Protocol deviation coded term	Treatment A	Treatment B	Treatment C	Total
Any type	2 (8.7%)	1 (5.0%)	3 (13.0%)	6 (9.1%)
Treatment deviations	2 (8.7%)	0	3 (13.0%)	5 (7.6%)
Procedure deviations	0	1 (5.0%)	0	1 (1.5%)
Minor Any type	12 (52.2%)	13 (65.0%)	16 (69.6%)	41 (62.1%)
InEx criteria not met but subject entered treatment	0	1 (5.0%)	0	1 (1.5%)
Treatment deviations	1 (4.3%)	3 (15.0%)	1 (4.3%)	5 (7.6%)
Time schedule deviations	8 (34.8%)	6 (30.0%)	7 (30.4%)	21 (31.8%)
Procedure deviations	10 (43.5%)	10 (50.0%)	13 (56.5%)	33 (50.0%)
Any type	12 (52.2%)	13 (65.0%)	16 (69.6%)	41 (62.1%)
InEx criteria not met but subject entered treatment	0	1 (5.0%)	0	1 (1.5%)
Treatment deviations	3 (13.0%)	3 (15.0%)	3 (13.0%)	9 (13.6%)
Time schedule deviations	8 (34.8%)	6 (30.0%)	7 (30.4%)	21 (31.8%)
Procedure deviations	10 (43.5%)	10 (50.0%)	13 (56.5%)	33 (50.0%)

Request:

Please tell us which data is used in following table.



Motivation



- Who was the developer?
- Where can I find the files?
- How was the derivation done?
- What data was used on that table?
- Which files belongs to the study?





Motivation

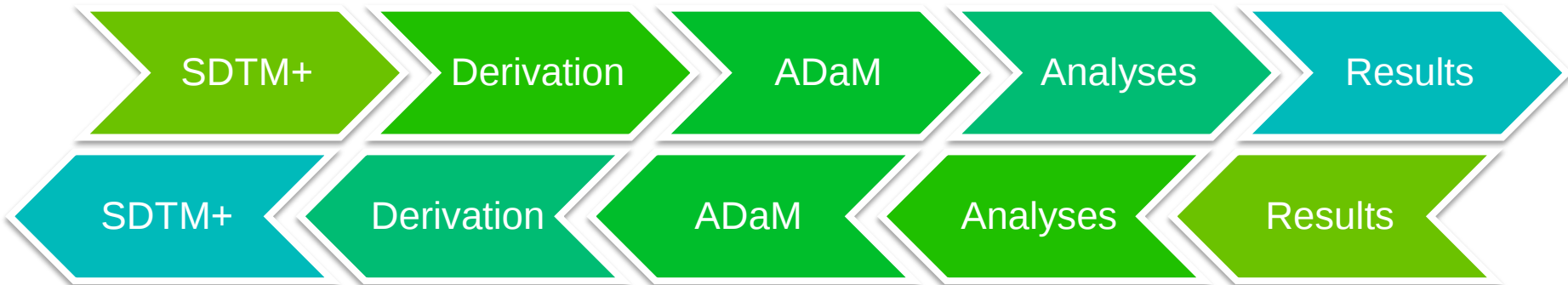


Knowledge about:

- Study
- Table
- Process chain clinical trial analyses

Identifying all information

- trace backwards





Collect information

Table: Number of subjects with protocol deviations by category and type (Safety analysis set)

Protocol	Treatment A	Treatment B	Treatment C	Total
Name	Typ			
I-as.sas	SAS-Datei			
I-cm.sas	SAS-Datei	(5.0%)	3 (13.0%)	6 (9.1%)
I-dm.sas	SAS-Datei		3 (13.0%)	5 (7.6%)
I-ds.sas	SAS-Datei			1 (1.5%)
I-ecog.sas	SAS-D	DVSEQ Sequence Number	SEQ Sponsor Defined Analysis Sequence Number	ASEQ Analysis Sequence Number
I-eff.sas	SAS-D		DVSPID Sponsor-Define Identifier	DVTERM Protocol Deviation Term
I-eg.sas	SAS-D			DVDEC Protocol Deviation Coded T
I-ex.sas	SAS-D	66	1	66
I-fail.sas	SAS-D	67	2	67
I-lb.sas	SAS-D	68	3	68
I-osaf.sas	SAS-D	69	1	69
I-pd.sas	SAS-D	70	2	70
I-vs.sas	SAS-D	71	4	71
m_byplot.sas	SAS-D	72	1	72
m_display_timeto	SAS-D	73	2	73
t-ae.sas	SAS-D	74	3	74
t-aelb.sas	SAS-D	75	1	75
t-bf.sas	SAS-D	76	1	76
t-cm.sas	SAS-D	77	1	77
t-dm.sas	SAS-D	78	2	78
t-ds.sas	SAS-D	79	1	79
t-ecog.sas	SAS-D	80	1	80
t-eff.sas	SAS-D			
t-eg.sas	SAS-D			
t-ex.sas	SAS-D			
t-lb.sas	SAS-D			
t-mh.sas	SAS-D			
t-sae.sas	SAS-D			

```

4969 DATA change;
4970   merge
4971   by P
4972   RUN;
4973   DATA ads.aeall(LABEL=Adverse events);
4974   SET change;
4975   RUN;

```



Collect information



Conclusion

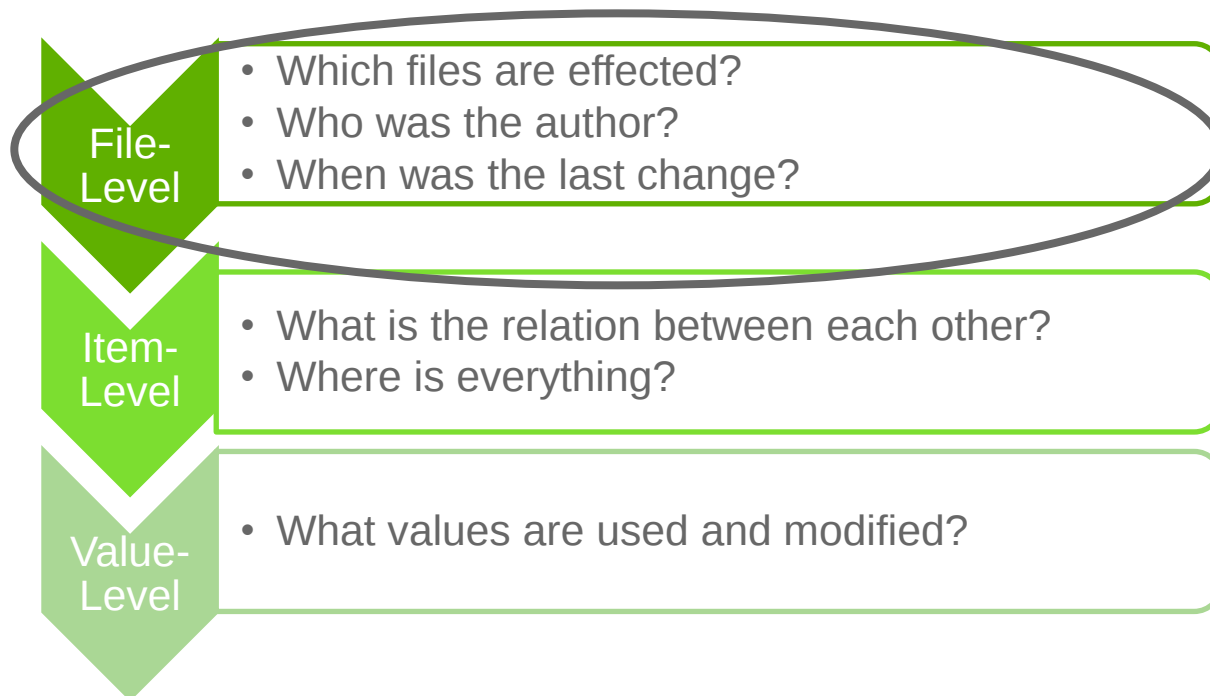
Using Traceability



Traceability

“Traceability describes the ability to verify the **origin, location, or application** of an **item** by means of documented recorded identification.

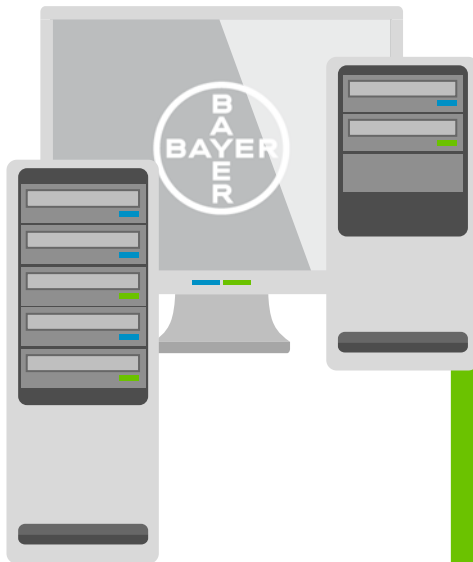
Traceability facilitates **transparency**, which is an **essential component** in building confidence in a result or conclusion.”¹



¹ <http://www.dddmag.com/articles/2012/03/ensuring-traceability-clinical-information>
Author: Michael Whitworth, last checked: 30.04.2014



System Logging Functionality



Audit
Access
Objects

**File-Level
Traceability**



System Logging Functionality

TUSC → no Prerequisites necessary, log all file operations from operating system

```
open("../pgms/t-dv.sas", O_RDONLY|0x800, 0666)=12
```

```
open("../data/ads/addv.sas7bdat", O_RDONLY|0x800, 0666)=13
```

```
close(13)=0
```

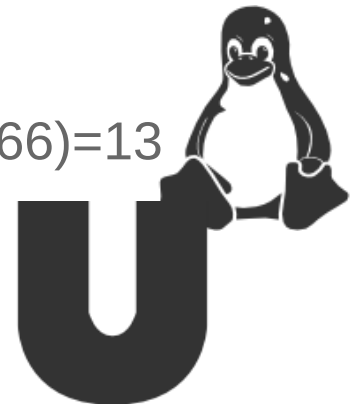
```
open("../data/ads/adsl.sas7bdat", O_RDONLY|0x800, 0666)=13
```

```
close(13)=0
```

```
open("../results/t-dv.lst",  
O_RDWR|O_CREAT|O_TRUNC|0x800, 0666)=13
```

```
close(13)=0
```

```
close(12)=0
```





System Logging Functionality

RTRACE

was developed for debugging SAS®-System

→ start with `-rtrace All`

→ `OPTION RTRACELOC = "Path/to/dir/location.rtrace"`

File referenced: `.../pgms/t-dv.sas`

File opened: `.../pgms/t-dv.sas`

File opened: `.../data/ads/addv.sas7bdat`

File closed: `.../data/ads/addv.sas7bdat`

File opened: `.../data/ads/adsl.sas7bdat`

File closed: `.../data/ads/adsl.sas7bdat`

File closed: `.../results/t-dv.lst`

File closed: `.../pgms/t-dv.sas`





File-Level Traceability

- Who was the developer?
 - ✓ File Owner
- Where can I find the files?
 - ✓ Path of all files
- Which files belongs to the study?
 - ✓ All effected files are listed
- How was the derivation done?
- What data was used for that table?





Code-Parsing – Item-Level

Knowing all used files → possibility to parse all necessary SAS-Programs

SAS-Code

SAS-Code-Interpretation

DATA change; —————→ Temporary Dataset **change**

merge tempdata.ae —————→ Created by merge from **ae** and **ads.adsl**
ads.adsl

(keep=SUBJID AGE SEX); —→ But only using SUBJID AGE and SEX from
by SUBJID; ads.adsl

RUN;

DATA ads.aeall(LABEL=Adverse events); —→ Permanent Dataset **ads.aeall**

SET change; —————→ Created from temporary dataset **change**

RUN;



Traceability Effect



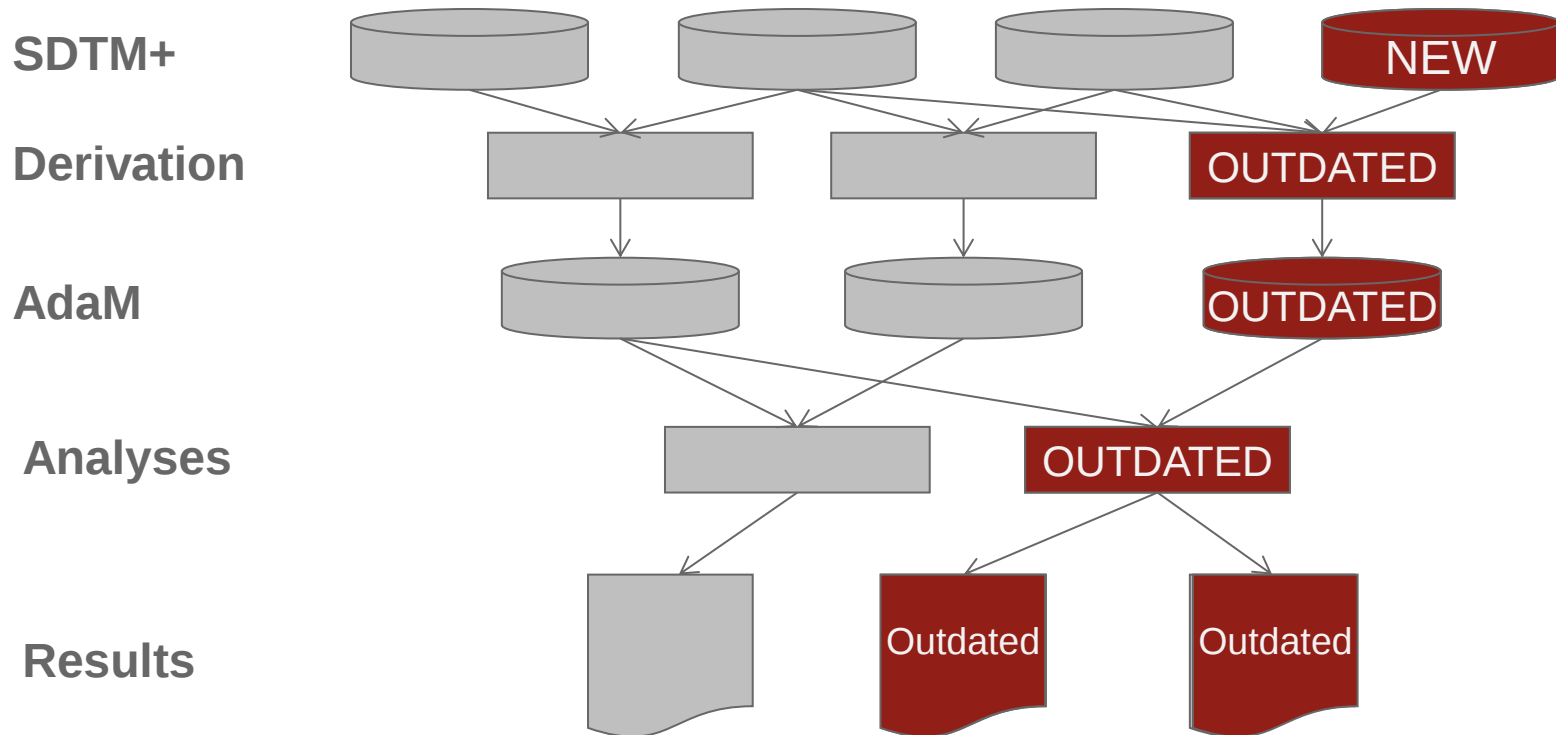
- Impact Analysis
 - method to identify the consequence of modifications



Traceability Effect

- Impact Analysis

→ method to identify the consequence of modifications





Traceability Effect



- Impact Analysis
 - method to identify the consequence of modifications
- Standard Checks
 - Loose ends/beginnings
 - Naming Conventions
- Fast Answers to Requests

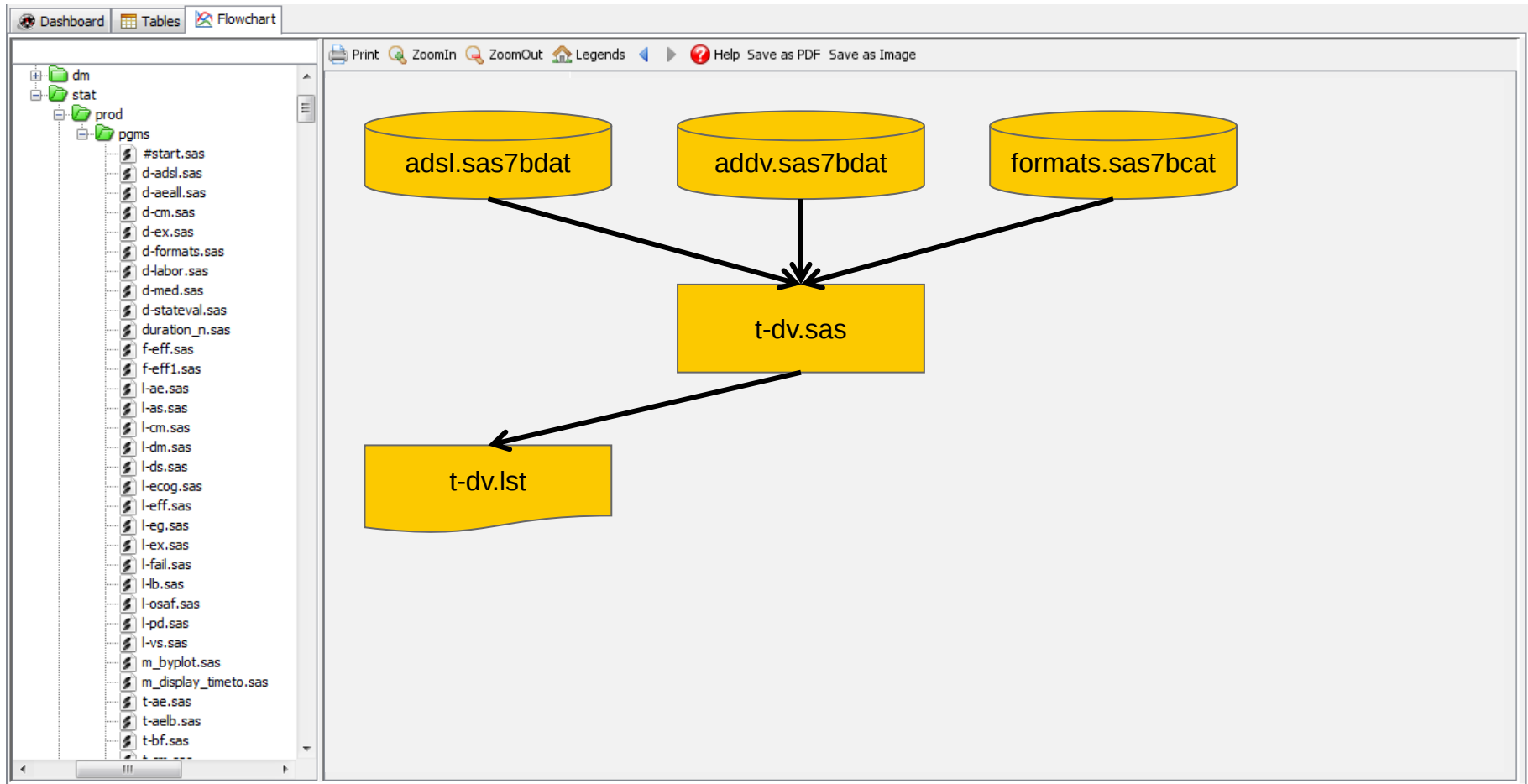


AirTracer – lighten up clinical trials

AirTracer - Demonstration

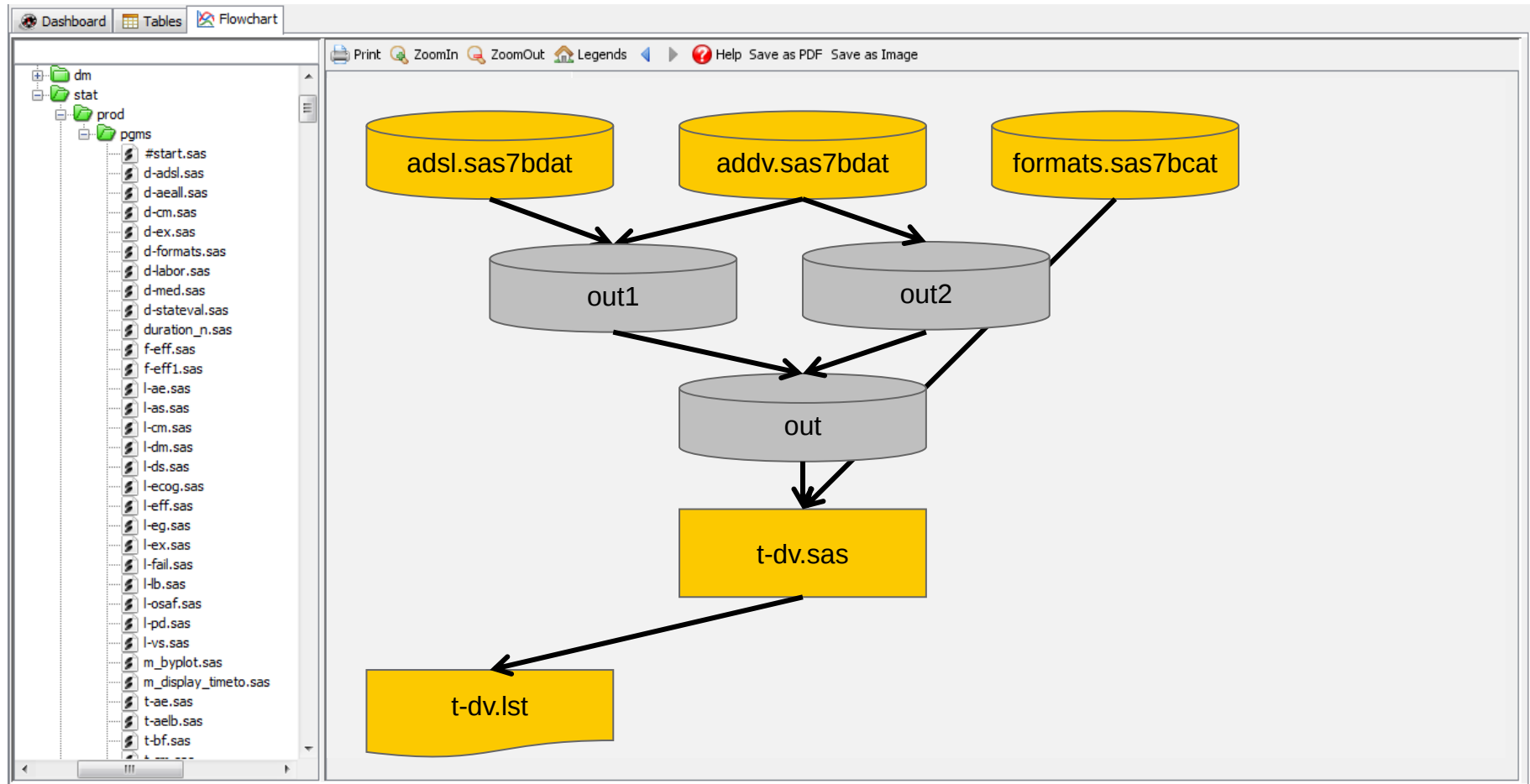


AirTracer – lighten up clinical trials



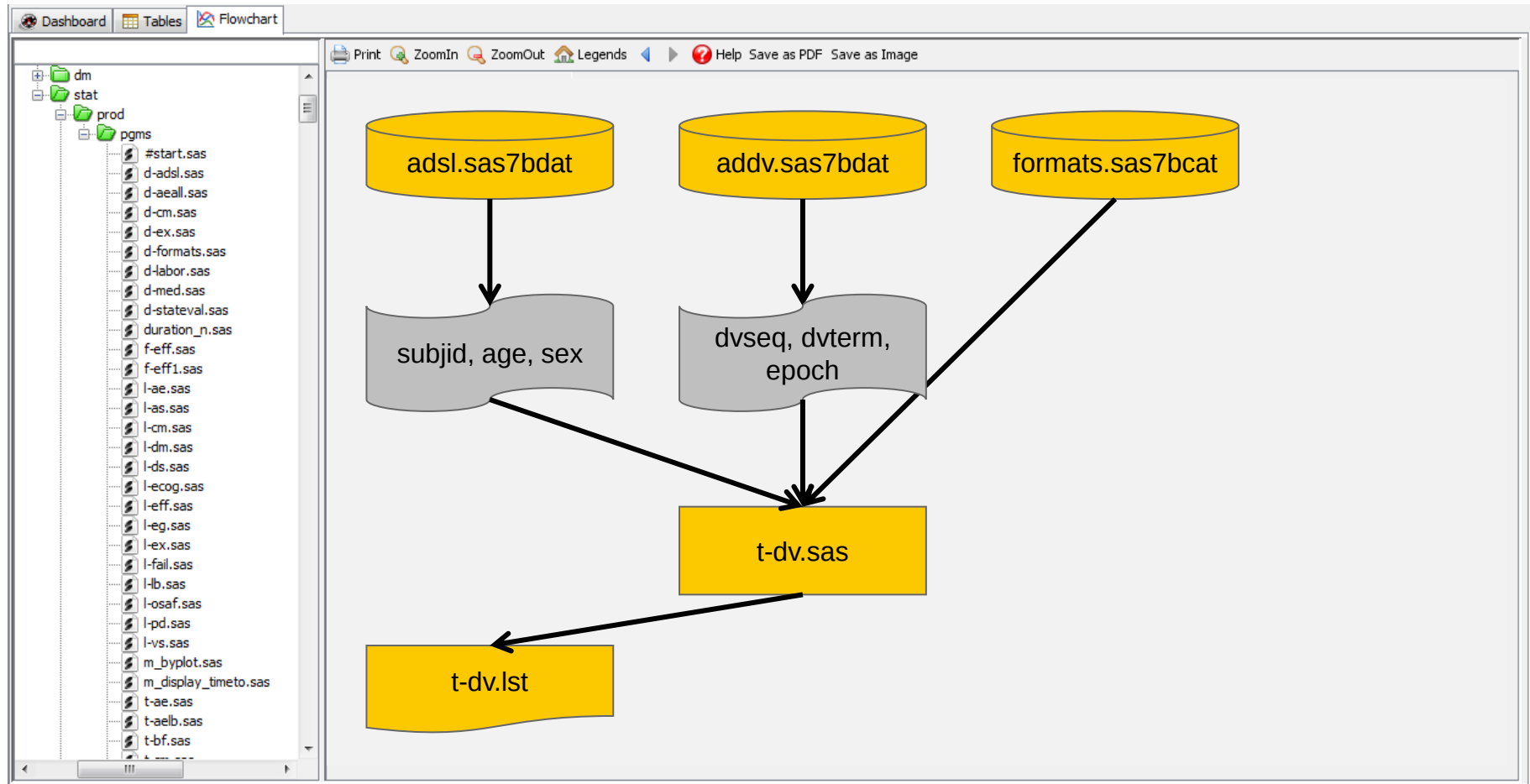


AirTracer – lighten up clinical trials





AirTracer – lighten up clinical trials





Summing-Up



- AirTracer JAVA written solution to enable a look into clinical trial analysis
- File-Level Traceability is 100% reproduced
- Problems
 - SAS-Macro Language hard to maintain
 - Full traceability not possible without user interaction(e.g. program header)

Advantages

- Draw an easy understandable Flowchart
- Fast Answers regarding to agency request are possible
- Helps user to understand an old study faster and easier
- Nice support for validation

Challenges

- Item-Level Traceability is not in all cases 100% exact
- SAS-Code Parsing needs time
- Possibility of type one error

References

1. <http://www.dddmag.com/articles/2012/03/ensuring-traceability-clinical-information> Author: Michael Whitworth, last checked: 30.04.2014
2. <http://www.phusewiki.org/docs/2012/PAPERS/RG/RG05.pdf> Author: Elena Glathe, last checked: 30.04.2014
3. <http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm070289.pdf> last checked: 30.04.2014
4. http://www.phusewiki.org/wiki/index.php?title=Traceability_and_Data_Flow last checked: 30.04.2014



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Thanks for your Attention

