

**AUTOMATE OR SUFFER
BY
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May 2013



Automatic annotations Overview



Our Background

Annotations,
but why?

Prerequisites

Examples:
The good, the bad
And the truly ugly

Technicalities:
Importing and
working with
annotations in
SAS

S&A:
Handling the
bad

Future
considerations

Main motivation

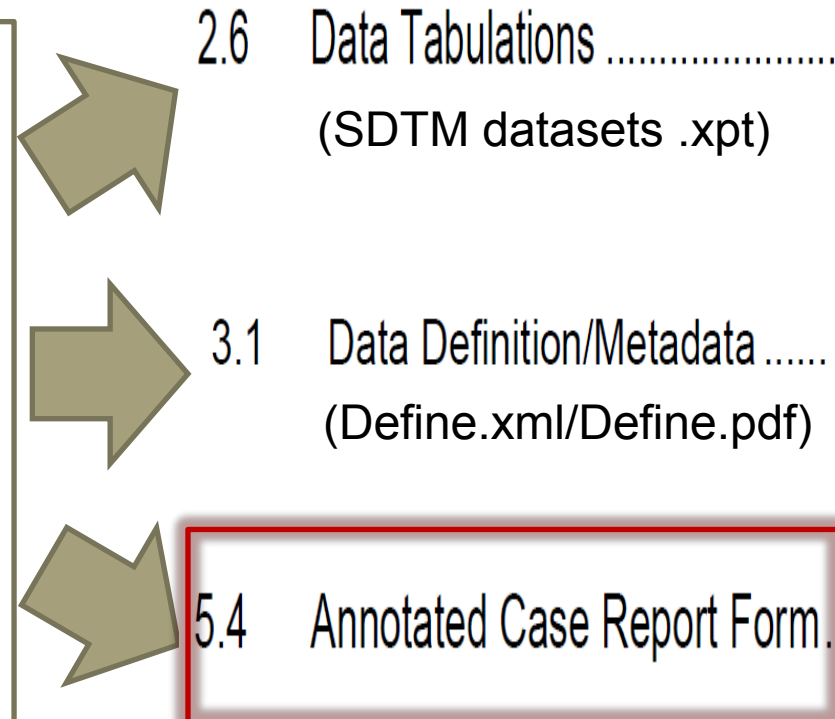
Annotations,
but why?



Study Data Specifications

July 18, 2012

Version 2.0



Annotations,
but why?



Secondary motivation

AEACN	AEACN	NSAEREAC	AE	AEACN
AEACN	AEACN	SAE_201	AE	AEACN
AEACNOTH	AEACNOTH	SAE_201	AE	AEACNOTH
AECTMYN	AECTMYN	NSAEREAC	AE	AECTMYN
AEDUR	AEDUR	NSAEREAC	AE	AEDUR
AEDUR	AEDUR	SAE_201	AE	AEDUR
AEENDTC	AEENDTC	NSAEREAC	AE	AEENDTC
AEENDTC	AEENDTC	SAE_201	AE	AEENDTC
AEOUTCOM	AEOUTCOM	NSAEREAC	AE	AEOUT
AEOUT	AEOUT	SAE_201	AE	AEOUT
AEREL	AEREL	NSAEREAC	AE	AEREL
AEREL	AEREL	SAE_201	AE	AEREL
AERELNST	AERELNST	NSAEREAC	AE	AERELNST
SER_CANC	SER_CANC	SAE_201	AE	AESCAN
SER_CONG	SER_CONG	SAE_201	AE	AESCONG
SER_DISA	SER_DISA	SAE_201	AE	AESDISAB
SER_DEAD	SER_DEAD	SAE_201	AE	AESDTH
AESER	AESER	NSAEREAC	AE	AESER
SERIOUS	SERIOUS	SAE_201	AE	AESER
AEINTENS	AEINTENS	NSAEREAC	AE	AESEV
AESEV	AESEV	SAE_201	AE	AESEV
SER_HOSP	SER_HOSP	SAE_201	AE	AESHOSP
SER_RISK	SER_RISK	SAE_201	AE	AESLIFE
SER_MEDS	SER_MEDS	SAE_201	AE	AESMIE
SER_ODOS	SER_ODOS	SAE_201	AE	AESOD

VS

Adverse Event Report No. AE.AESPID

1. ADVERSE EVENT AE.AETERM
Additional Description (if necessary):
SUPPAE.REACCODE CO.COVAL

2. Intensity: ☐ Mild ☐ Moderate ☐ Severe AE.AESEV

3. Adverse Event Start: AE.AESTDTC AE.AEDUR AE.AEDUR
Duration of Event if Less than 1 Day: ☐ Secs ☐ M
Indicate Time from Most Recent Dose of Study Drug to Onset of Event: SUPPAE.AEONSTIM
Study Drug Dose and Schedule at Onset of Event: SUPPAE.AEONSDOS

4. Did Event Require Treatment with Counteractive Medication (including IV)? ☐ No ☐ Yes, specify on Concomitant Medication page. AE.AECONTRT

5. Investigator's Causality: Relationship to Study Drug
☐ Definitely Related ☐ Probable ☐ Possible ☐ Unlikely* ☐ Not Related*
* If unlikely, or not related, alternative explanation is (Check one most likely choice)
☐ Concomitant Medication, specify on Concomitant Medication page
☐ Concurrent Illness, specify below
☐ Other Known or Suspected Cause, specify below
AE.AERELNST

6. Action Taken with Study Drug (check only one): ☐ Reduced dose due to event SUPPAE.AENEWDOS ☐ Increased dose due to event SUPPAE.AENEWDOS ☐ Therapy unchanged due to event

7. Outcome: AE.AEOUT

Annotations,
but why?



Prologue

Dirk Spruck and Monika Kawohl (2004): Write FDF*, import to PDF. Move manually. Multiply to copies of page.

Legacy studies:
CRF already annotated

Export-Change-Import

Newer EDMs:
Annotated CRF as PDF

Other requirements

*: See PDF documentation

Prerequisites

What's required

Documentation of mappings

A reasonably annotated crf

A bit of patience, sas and a minimum of programming skills

Examples:
The good, the bad
And the truly ugly



Examples: The good ... or at least OK

DATASET:
AEDS

AED MEDICATION HISTORY (Within the last two years)					
Medication	Start Date (mm/dd/yy)	Stop Date (mm/dd/yy)	Medication	Start Date (mm/dd/yy)	Stop Date (mm/dd/yy)
1. AEDTEXT	AEDSTDTC	AEDENDTC		///	///
2.	///	///	6.	///	///
3.	///	///	7.	///	///
4.	///	///	8.	///	///

Spelling
errors

Algorithm for
pairing dataset
and fieldname?

DATASET:
AEDHX

Is the patient experiencing any adverse signs and symptoms related to their current AED therapy? ☐ No ☐ Yes*

AEDHXYN

* If YES, indicate below AED name and associated adverse signs and symptoms:

AED Name	Adverse Signs & Symptoms
1. AEDTEXT	AETEXT
2.	

Easy to work
with the
annotations

Examples:
The good, the bad
And the truly ugly



Examples: The bad, is also the best

Autogenerated

Form: Completion/Withdrawal

Generated On: 03 Nov 2010 18:07:30

Date of completion or withdrawal: ①

Date of Last Dose: ②

Did the patient complete the trial as planned? Yes ☐ ③
No ☐

Adverse Event ④

If yes, identify the Primary AE Description: ⑤

A single GTCS (If GTCS were not previously reported) or a new onset seizure types ⑥

ILAE Code: ⑦
Partial seizures ☐
Simple partial seizures ☐
Complex partial seizures ☐
Simple partial onset followed by ☐

No Spelling errors

Only one dataset per page

Form: Completion/Withdrawal

Generated On: 03 Nov 2010 18:07:30

	Field Name	Data Type	Field Label	Units	Pre-Filled Values	Include Field OID
①	CWDC	dd MMM yyyy	Date of completion or withdrawal:			CWDC
②	CWLD	dd MMM yyyy	Date of Last Dose:			CWLD
③	CWCOMPL	\$1	Did the patient complete the trial as planned?			CWCOMPL
④	CWAE	1	Adverse Event			CWAE
⑤	PRIMAE	\$50	If yes, identify the Primary AE Description:			PRIMAE

No annotations to read, so how do we proceed?

Examples:
The good, the bad
And the truly ugly



Examples: The truly ugly

Date of diagnosis of refractory partial epilepsy				DDIAGRPE 3.1.14			
Severity of disease				SEVER 35			
Not severe ☐ N		Mildly severe ☐ M		Very severe ☐ V			
SPECIF 3.8.14							
Are there any relevant diseases or illnesses in the subject's medical history? ☐ No ☐ Yes							
♦ If YES, please specify.							
Medical event/disease	Date started	Ongoing at Screening visit	if NO, date ended				
(day) (month) (year)	(day) (month) (year)	No Yes	(day) (month) (year)				
[1] HIST1 3.1.14	DSTART1 3.1.14	N ☐ Y ☐	DSTOP1 3.1.14				
[2] HIST2 3.1.14	DSTART2 3.1.14	N ☐ Y ☐	DSTOP2 3.1.14				
[3] HIST3 3.1.14	DSTART3 3.1.14	N ☐ Y ☐	DSTOP3 3.1.14				
[4] HIST4 3.1.14	DSTART4 3.1.14	N ☐ Y ☐	DSTOP4 3.1.14				

What to do?

Export annotations

Very long record length

Very long record length

Delimiter: 'endobj'

Exporting FDF from SAS

Required elements:
Header
Catalog
Annotations
Trailer

Can PROC TEMPLATE
be used?

```
2 0 obj
<<
  /Type /Annot
  /Subtype /FreeText
  /Rect [ 1 598.509 91 612.509 ]
  /C [1 1 1 ]
  /DA ([1 0 0] r /Helv 10 Tf)
  /BS << /w 1 >>
  /F 4
  /Contents (SUPPDM.SCRNO)
  /Page 2
>>
endobj
|
```

S&A:
Handling the
bad



Importing standard PDF

```
/Filter/FlateDecode/First 22/Length 258,  
-45!40(ms«-|Ú¿iæqé@-h«³f†Y!|-`È%ã¥!DV«bu|Z  
/Annots[516 0 R 517 0 R 518 0 R 519 0 R  
,`w·läm3~<8- AN,i- æiÄaîð×xU“»g`»}\  
,3*“>Q«EFTÖ-+fT-xT«xV-AfThz>Z5«EY£iÖEöZ8:  
X«(ç%ä:J t«“-`f·äz-|@ÜÖ-«îÖÖ`«E-ä×fj)  
/Filter/FlateDecode/First 84/Length 258,  
-45!40(ms«-|Ú¿iæqé@-h«³f†Y!|-`È%ã¥!DV«bu|Z  
/Annots[516 0 R 517 0 R 518 0 R 519 0 R  
,`w·läm3~<8- AN,i- æiÄaîð×xU“»g`»}\  
,3*“>Q«EFTÖ-+fT-xT«xV-AfThz>Z5«EY£iÖEöZ8:  
X«(ç%ä:J t«“-`f·äz-|@ÜÖ-«îÖÖ`«E-ä×fj)  
/Filter/FlateDecode/First 58/Length 258,  
-45!40(ms«-|Ú¿iæqé@-h«³f†Y!|-`È%ã¥!DV«bu|Z  
/Annots[516 0 R 517 0 R 518 0 R 519 0 R  
,`w·läm3~<8- AN,i- æiÄaîð×xU“»g`»}\  
,3*“>Q«EFTÖ-+fT-xT«xV-AfThz>Z5«EY£iÖEöZ8:  
X«(ç%ä:J t«“-`f·äz-|@ÜÖ-«îÖÖ`«E-ä×fj)  
/Filter/FlateDecode/First 54/Length 304,  
-45!40(ms«-|Ú¿iæqé@-h«³f†Y!|-`È%ã¥!DV«bu|Z  
/Annots[516 0 R 517 0 R 518 0 R 519 0 R  
,`w·läm3~<8- AN,i- æiÄaîð×xU“»g`»}\  
,3*“>Q«EFTÖ-+fT-xT«xV-AfThz>Z5«EY£iÖEöZ8:  
X«(ç%ä:J t«“-`f·äz-|@ÜÖ-«îÖÖ`«E-ä×fj)  
/Filter/FlateDecode/First 46/Length 299,  
-45!40(ms«-|Ú¿iæqé@-h«³f†Y!|-`È%ã¥!DV«bu|Z  
/Annots[516 0 R 517 0 R 518 0 R 519 0 R  
,`w·läm3~<8- AN,i- æiÄaîð×xU“»g`»}\  
,3*“>Q«EFTÖ-+fT-xT«xV-AfThz>Z5«EY£iÖEöZ8:  
X«(ç%ä:J t«“-`f·äz-|@ÜÖ-«îÖÖ`«E-ä×fj)  
/Filter/FlateDecode/First 14/Length 237,  
-45!40(ms«-|Ú¿iæqé@-h«³f†Y!|-`È%ã¥!DV«bu|Z  
/Annots[516 0 R 517 0 R 518 0 R 519 0 R  
,`w·läm3~<8- AN,i- æiÄaîð×xU“»g`»}\  
,3*“>Q«EFTÖ-+fT-xT«xV-AfThz>Z5«EY£iÖEöZ8:  
X«(ç%ä:J t«“-`f·äz-|@ÜÖ-«îÖÖ`«E-ä×fj)
```

Not readily
readable

```
42.000" rotate="0">  
3.779,770.669">  
770.669">  
59.509,243.229,770.669" size="11.160">0</  
59.509,248.229,770.669" size="11.160">1</  
59.509,253.229,770.669" size="11.160">5</  
59.509,258.229,770.669" size="11.160">7</  
59.509,260.729,770.669" size="11.160"> </  
59.509,265.729,770.669" size="11.160">1</  
59.509,270.729,770.669" size="11.160">3</  
59.509,275.729,770.669" size="11.160">1</  
59.509,280.729,770.669" size="11.160">8</  
59.509,285.729,770.669" size="11.160">1</  
59.509,292.949,770.669" size="11.160">A</  
59.509,295.449,770.669" size="11.160"> </  
59.509,302.669,770.669" size="11.160">v</  
59.509,307.109,770.669" size="11.160">e</  
59.509,310.439,770.669" size="11.160">r</  
59.509,314.329,770.669" size="11.160">s</  
59.509,317.109,770.669" size="11.160">i</  
59.509,317.109,770.669" size="11.160">o</  
59.509,317.109,770.669" size="11.160">n</  
59.509,317.109,770.669" size="11.160"> </  
59.509,317.109,770.669" size="11.160">3</  
59.509,317.109,770.669" size="11.160"> </  
59.509,317.109,770.669" size="11.160">0</  
59.509,317.109,770.669" size="11.160">0</  
59.509,349.609,770.669" size="11.160"> </  
59.509,352.939,770.669" size="11.160"> </  
59.509,355.439,770.669" size="11.160"> </  
59.509,360.999,770.669" size="11.160">P</  
59.509,368.219,770.669" size="11.160">D</  
59.509,373.779,770.669" size="11.160">F</
```

Example:
PDFMiner by
Yusuke Shinyama

Future Considerations



Next step

Colour coding

Popups for lengthier explanations

Annotating values

Other ideas?

0157 13081A Version 3.06 PDF
Form: Completion/Withdrawal
Generated On: 13 Mar 2013 14:43:57

Field Name	Data Type	Field Label	Units	Pre-Filled Value	Include Field OED
SUPPOS.CWLPHOC	SUPPOS.LYPSOYC	Date of last contact			CWLPHOC
DS.DTERM	100	CWDEATH	1	Patient Died	CWDEATH
SUPPOS.AEDTHRES	DEASP	550		Cause of death	CWDEATH
SUPPOS.CWDEALOC	DEALALC	44 MM		Date of death	CWDEALC
DS.DTERM	100	CWWCOC	1	Voluntarily Withdraw	CWWCOC
DS.DTERM	100	CWPHYS	1	Physician Decision	CWPHYS
SUPPOS.CWPHYSOC	PHYSOC	550		Physician Decision, specify:	CWPHYS
DS.DTERM	100	CWSPON	1	Sponsor Decision	CWSPON
SUPPOS.CWSPONSP	SPONSP	550		Sponsor Decision, specify:	CWSPONSP
DS.DTERM	100	CWPRG	1	Pregnancy	CWPRG
DS.DTERM	100	CWINDEX	1	Did not meet inclusion or not evaluation criteria	CWINDEX

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