

A photograph of the Tower Bridge in London, with its two massive stone towers and suspension cables. The bridge's bascules are raised, and a large yellow duck is floating in the water in front of it. The Shard is visible in the background.

Automating Production of the blankcrf.pdf

Presenter Joseph Rowley,
Paper Author Walter Hufford,
London PhUSE 2014

Blank Case Report Form

(blankcrf.pdf)

 NOVARTIS Study	ID	SCREENING
	Center No.	Subject No.
Visit Name		

Demography

Before entering data, please check CCG for information regarding privacy laws for your country.

Is collection of actual date of birth allowed? ☐ No ☐ Yes

Date of Birth
DD-MON-YYYY

Year of Birth

Calculated Age YEARS

Is collection of initials allowed? ☐ No ☐ Yes

Subjects Initials

Sex ☐ Male ☐ Female

Is Subject of Child Bearing Status

Race

Specify Race

Ethnicity

Source of Subject Referral

Specify Other Source of Subject Referral

DMG02

Epoch Screening	Document Number	Subevent#	Page Number 3
Verified ☐ Approved ☐ Locked ☐ Frozen ☐	Page Name DEMOGRAPHY	Status	Version 1

Annotating the Case Report form

- Critical Component of the NDA Submission

- Source Data Domain

DM = Demographics

- Variable Name

BRTHDTC

- Controlled Terminology

Annotated Blank Case Report Form

(blankcrf.pdf)

DM = Demographics SC = Subject Characteristics

 Study GURDREPUS STUDYID	ID Center No. USUBJID Subject No.	SCREENING Visit Name [NOT SUBMITTED]
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Demography

Before entering data, please check CCG for information regarding privacy laws for your country.

Is collection of actual date of birth allowed? ☐ No ☐ Yes [NOT SUBMITTED]

Date of Birth **BRTHDTC**
DD-MON-YYYY

Year of Birth [NOT SUBMITTED]

Calculated Age YEARS **AGEU**

Is collection of initials allowed? ☐ No ☐ Yes [NOT SUBMITTED]

SCTEST Subjects Initials **SCORRES when SCTESTCD = SBJINIT**

Sex ☐ Male ☐ Female **SEX**

SCTEST Is Subject of Child Bearing Status **SCORRES when SCTESTCD = CHDBER**

Race **RACEOR in SUPPDM**

RACESY in SUPPDM Specify Race

Ethnicity **ETHNICOR in SUPPDM**

SCTEST Source of Subject Referral **SCORRES when SCTESTCD = SRCRF**

Specify Other Source of Subject Referral

SRCRFSY in SUPPSC

18
Annotations
81 page document

Manual Annotation of the blankcrf.pdf

Performed in Adobe Acrobat Using the Comment Tool

CAIN457F2305 eCRF layout Version 2 0.pdf - Adobe Acrobat

File Edit View Window Help Novartis Signing

Create

29 / 982 78.6%

Tools Comment

NOVARTIS Study	ID Center No.	Subject No.	SCREENING Visit Name
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Demography

Before entering data, please check CCG for information regarding privacy laws for your country.

Is collection of actual date of birth allowed? ☐ No ☐ Yes

Date of Birth **BRHDTTC**

Year of Birth

Calculated Age YEARS

Is collection of initials allowed? ☐ No ☐ Yes

Subjects Initials

Sex ☐ Male ☐ Female

Is Subject of Child Bearing Status

Race

Specify Race

Ethnicity

Source of Subject Referral

Specify Other Source of Subject Referral

Annotations

Drawing Markups

Review

Comments List (1)

Find

ROWLEJ01

Page 29 10/9/2014 10:25:05 PM

BRHDTTC

Automating Annotation with Adobe Acrobat

Adobe Acrobat annotation attributes

F2305_ALL_BOOKMARKS (2).pdf - Adobe Acrobat

File Edit View

DM = Demographics SC = Subject Characteristics

 NOVARTIS Study GURDREPUS	ID	Center No.	Subject No.	SCREENING Visit Name [NOT SUBMITTED]
	STUDYID		USUBJID	

Demography

Before entering data, please check CCG for information regarding privacy laws for your country.

Is collection of actual date of birth allowed? ☐ No ☐ Yes [NOT SUBMITTED]

Date of Birth BRTHDTC
DD-MON-YYYY

Year of Birth [NOT SUBMITTED]

Calculated Age YEARS AGE AGEU

Is collection of initials allowed? ☐ No ☐ Yes [NOT SUBMITTED]

SCTEST Subjects Initials SCORRES when SCTESTCD = SBJINIT

Sex ☐ Male ☐ Female SEX

SCTEST Is Subject of Child Bearing Status SCORRES when SCTESTCD = CHDBER

Race RACEOR in SUPPDM

RACESY in SUPPDM Specify Race

Ethnicity ETHNICOR in SUPPDM

SCTEST Source of Subject Referral SCORRES when SCTESTCD = SRCRF

Specify Other Source of Subject Referral

SRCRFSY in SUPPSC

[Everything below the line: NOT SUBMITTED]

Consent	Epoch Screening	Document Number	Subevent#	Page Number 3
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Screening Phase

NCDS
Page 2 Indeterminate

NOVARTIS

Automation repository

- Rather than create a single re-usable FDF file a better approach is to create a repository of annotations and associated attributes which is used in the creation of study-specific FDF files
- Repository containing a few required annotation attributes is easy to set-up and maintain
- Simple SAS® programs are created to:
 - (1) load individual annotation attributes to the repository
 - (2) select study-specific appropriate annotations from the repository, and
 - (3) produce study-specific FDF files
- As existing CRF pages are updated or new standard CRF pages are implemented the repository is easily updated
- SAS programs only require updating if the FDF file structure changes

Building a Repository

CRF

CM2G02

Surgeries and Medical
Procedures

CMG02

Prior and Concomitant
Medications

IEG03

Inclusion Exclusion

SVG02

Study visit

FDF

CM2G02.fdf

CMG02.fdf

IEG03.fdf

SVG02.fdf

SAS Repository

	Annotation Text	Coordinates of Annotation Text	CRF Page	Domain Level	Domain Name
21	CMTRT	688 384 728 398	CM2G02	1	CM
22	CMDOSE	706.984 358.833 754.984 372.833	CM2G02	1	CM
23	CMDOSE	266 356 314 370	CM2G02	1	CM
24	CMINDC	686 332 734 346	CM2G02	1	CM
25	CMSTDTC	454 307 510 321	CM2G02	1	CM
26	CMONGO in SUPPCM	586 296 706 310	CM2G02	1	CM
27	CMENDTC	258 271 314 285	CM2G02	1	CM
28	CM = Concomitant Medications	59 3296 585 432 216.988 599.442	CM2G02	1	CM
29	[NOT SUBMITTED]	506 424 614 441	CM2G02	.	.
30	[Everything below the line: NOT SUBMITTED]	271 85 490 100	CM2G02	.	.
31	STUDYID	174 523 230 537	CMG02	1	CM
32	USUBJID	334 520 390 534	CMG02	1	CM
33	CMCAT	421.306 396.861 461.306 410.861	CMG02	1	CM
34	CMTRT	625 159 426 939 665 159 440 939	CMG02	1	CM
35	CMINDC	226 334 274 348	CMG02	1	CM
36	CMSTDTC	420.16 313.0 476.16 327.0	CMG02	1	CM
37	CMENDTC	210 281 266 295	CMG02	1	CM
38	CMONGO in SUPPCM	624 669 284 661 743.669 298.661	CMG02	1	CM
39	RESDC in SUPPCM	653.167 245.339 764.167 259.339	CMG02	1	CM
40	CMDOSE	369 502 223.673 417.502 237.673	CMG02	1	CM
41	CMDOSE	497 211 545 225	CMG02	1	CM
42	CMDOSEFRQ	439.0 187 669 503.0 201.669	CMG02	1	CM
43	CMROUTE	563.823 167.837 619.823 181.837	CMG02	1	CM
44	IDTHYCM = MEDICATIONS in SUPPCM	60.4333 494.1 251.132 509.1	CMG02	1	CM
45	CM = Concomitant Medications	57.5814 585.144 215.239 599.154	CMG02	1	CM
46	[NOT SUBMITTED]	457 448 565 466	CMG02	.	.
47	[Everything below the line: NOT SUBMITTED]	271 85 490 100	CMG02	.	.
48	STUDYID	174 523 230 537	IEG03	1	IE
49	USUBJID	334 520 390 534	IEG03	1	IE
50	IECAT	229.661 398.526 269.661 412.526	IEG03	1	IE
51	IETESTCD	514.988 350.387 578.988 364.387	IEG03	1	IE
52	IEORRES when IETESTCD = INCL01-INCL11, EXCL01-EXCL28	514.988 310.722 731.349 337.722	IEG03	1	IE
53	IE = Inclusion/Exclusion Criteria Not Met	57.8022 583.177 253.763 597.187	IEG03	1	IE
54	[NOT SUBMITTED]	502 633 442 004 610.633 459.004	IEG03	.	.
55	[Everything below the line: NOT SUBMITTED]	271 85 490 100	IEG03	.	.
56	[NOT SUBMITTED]	50.2913 402.272 158.291 420.272	IEG03	.	.
57	SV = Subject Visits	58 581 174 595	SVG02	1	SV
58	STUDYID	174 523 230 537	SVG02	1	SV
59	USUBJID	334 520 390 534	SVG02	1	SV
60	VISIT	654 520 694 534	SVG02	1	SV
61	SVSTDTC	434.212 469.192 490.212 483.192	SVG02	1	SV
62	[Everything below the line: NOT SUBMITTED]	271 85 490 100	SVG02	.	.

Automating Annotation programmatically using Forms Data Format (FDF) File.

Repository dataset

	A	B	C	D	E	F	G	H	I	J
1	CRFID	DOMAIN	ELEMENT	C1	C2	C3	C4	SUPP	CT	ORDR
2	DMG02	DM	DM = Demographics	58	581	162	595			1
3	DMG02	DM	STUDYID	174	523	230	537			1
4	DMG02	DM	USUBJID	334	520	390	534			1
5	DMG02	DM	[NOT SUBMITTED]	575	519	683	533			1
6	DMG02	DM	[NOT SUBMITTED]	386	450	494	464			1
7	DMG02	DM	BRTHDTC	386	430	442	444			1
8	DMG02	DM	[NOT SUBMITTED]	344	400	452	414			1
9	DMG02	DM	AGE				198			1
10	DMG02	DM	AGEU				198		UNIT	1
11	DMG02	DM	[NOT SUBMITTED]	384	362	492	376			1
12	DMG02	DM	SEX	410	320	434	334		SEX	1
13	DMG02	DM	RACEOR in SUPPDM	143	278	262	292	Y		1
14	DMG02	DM	RACESY in SUPPDM	108	259	227	273	Y		1
15	DMG02	DM	ETHNICOR in SUPPDM	548	239	683	253	Y		1
16	DMG02	DM	SRCRFSY in SUPPSC	309	175	437	189	Y		1
17	DMG02	SC	SC = Subject Characteristics	165	581	336	595			2
18	DMG02	SC	SCORRES when SCTESTCD = SBJINIT	361	342	556	357			2
19	DMG02	SC	SCTEST	156	341	204	355			2
20	DMG02	SC	SCORRES when SCTESTCD = CHDBER	540	299	735	313			2
21	DMG02	SC	SCTEST	75	298	123	312			2
22	DMG02	SC	SCTEST	107	220	155	234			2
23	DMG02	SC	SCORRES when SCTESTCD = SRCRF	536	218	731	232			2

```

if rx gt 0 and length GT 0 then do;
  call prxposn(rx, 1, start1, length);
  element=substr(_infile_,start1,length);
end;

```

```

call prxposn(rx, 1, start, length);
_coord=substr(_infile_,start,length);
end;

```

Using a Repository

CRF

CM2G02

Surgeries and Medical Procedures

CMG02

Prior and Concomitant Medications

IEG03

Inclusion Exclusion

SVG02

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35	CMINDC	226 334 274 348	CMG02	1	CM
36	CMSTDTC	420 16 313 0 476 16 327 0	CMG02	1	CM
37	CMENDTC	210 281 266 295	CMG02	1	CM
38	CMONGO in SUPPCM	524.669 296.861 743.669 308.861	CMG02	1	CM
39	RESDC	563.823 167.837 619.823 181.837	CMG02	1	CM
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60	VISIT	654 520 694 534	SVG02	1	SV
61	SVSTDTC	434.212 469.192 490.212 483.192	SVG02	1	SV
62	[Everything below the line: NOT SUBMITTED]	271 85 490 100	SVG02	.	.

Create study specific FDF

Study Specific Driver

Build FDF File for Study specific CRF

- Created for each new blankcrf.pdf
- Only Contains 2 Variables and is Used to identify which:
 - unique CRF pages are used
 - blankcrf.pdf page they appear on
- Template Created Same Time as Repository
 - CRFID and DOMAIN pre-populated
- End-user Only Needs to Identify Which Page a Unique CRFID is on

D12			
	A	B	C
1	CRFID	PAGE	
2	SVG02	1	
3	IEG03	2	
4			
5			
6			

Study specific FDF File

%FDF-1.2

1 0 obj

<< /FDF << /Annots [2 0 R 3 0 R 4 0 R 5 0 R 6 0 R 7 0 R 8 0 R 9 0 R 10 0 R 11 0 R 12 0 R 13 0 R 14 0 R 15 0 R 16 0 R 17 0 R 18 0 R] >> >>

endobj

2 0 obj

<</BS 21 0 R/C[0.0 1.0 1.0]/Contents(STUDYID)/DA(0 0 0 rg /Helv 12 Tf)/DS(font: Arial,sans-serif 9.0pt; text-align:left; color:##000000)/F 4/Page 0 /Rect[159.985 554.563 206.077 568.163]/Subj(TextBox)/Subtype/FreeText/T(NCDS)/Type/Annot>>

endobj

■ Produced Using a Simple* SAS Program

<</BS 21 0 R/C[1.0 1.0 1.0]/Contents(CRFID=SVG02)/Page 0 /DA(1 1 1 rg /Helv 12 Tf)/DS(font: Arial,sans-serif 9.0pt; text-align:left; color:##000000)/F 4/RC(<?xml style="font-size:9.0pt;text-align:left;color:##FFAA00 ;font-weight:normal;font-style:normal;font-family:Arial,sans-serif;font-stretch:normal"><p dir="ltr">CRFID=SVG02 </p></body>)/Rect[63.7056 14.444 197.171 29.0886]/Subj(Typewritten Text)/Subtype/FreeText/T(NCDS)/Type/Annot>>

■ Caution:

Endobj

..... • Header and body must align on number of annotations

12 0 obj

<</BS 21 0 R/C[0.0 1.0 1.0]/Contents(CRFID=IEG03)/Page 1 /DA(1 1 1 rg /Helv 12 Tf)/DS(font: Arial,sans-serif 9.0pt; text-align:left; color:##000000)/F 4/RC(<?xml style="font-size:9.0pt;text-align:left;color:##FFAA00 ;font-weight:normal;font-style:normal;font-family:Arial,sans-serif;font-stretch:normal"><p dir="ltr">CRFID=IEG03 </p></body>)/Rect[63.7056 14.444 197.171 29.0886]/Subj(Typewritten Text)/Subtype/FreeText/T(NCDS)/Type/Annot>>

• Less in header, annotations will be missing

Endobj

.....

18 0 obj

<</BS 21 0 R/C[0.0 1.0 1.0]/Contents(USUBJID)/DA(0 0 0 rg /Helv 12 Tf)/DS(font: Arial,sans-serif 9.0pt; text-align:left; color:##000000)/F 4/Page 1 /Rect[401.697 554.17 445.183 567.77]/Subj(TextBox)/Subtype/FreeText/T(NCDS)/Type/Annot>>

endobj

trailer

<< /Root 1 0 R >>

%%EOF

Conclusion

- Production of the blankcrf.pdf doesn't need to be Tedious and error prone

- With programmer ingenuity
 - CRF Standardization
 - Simplicity of the FDF file structure
 - You are only a few simple steps away from an accurate, consistent, automated blankcrf.pdf

Contact

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