PhUSE 2007

Paper PO04

Medical Safety Review Process

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ABSTRACT

Medical Safety Review (MSR) is a uniform process to facilitate safety review at an early stage.
The information will be provided to clinicians and statisticians by a single word document with hyperlinks to predefined components.

INTRODUCTION

The MSR process is conducted to identify, at an early stage, potential safety issues for ongoing trials. It facilitates safety review of the data by both clinicians and statisticians. This MSR Tool established a standard global process across the different franchises/teams. This process can start once the draft clinical safety and exposure data become available.
The scope covers data from demographics, safety parameters (adverse events, vital signs, ECG and laboratory), concomitant medication, medical history, disposition to exposure, and can be extended on the basis of trial-specific requirements.

CONCEPT

All review on the safety data will be directed from one single Word document. This document is a table of contents with bookmarks and hyperlinks to three main review components, being Safety Tables and Listings,
Subject Profiles Listings, and Graphical Subject Profiles. Because of the hyperlinks, it is a user-friendly and very accessible review tool for all kinds of users. Especially the Graphical Subject Profile is a powerful component of the tool. In these graphs, all safety data of each single subject are over time and provide a clear overview of all parameters of interest in just a couple of pages. This allows the user to identify possible relationships between events from different domains, e.g. the occurrence of an AE versus the timing of drug intake. Outliers and subjects at risk can be quickly identified via color-coding and symbol notation. Bookmarks can be predefined to prioritize the review for trial specific population of interests. A link to the full-text subject profile listings is available within the graphical subject profile, and vice versa.

COMPONENTS

All intermediate components described above are built using SAS.
The MSR process is established based on a set of in house macros, which provide a user-friendly setting to statistical programmers.
No SAS knowledge is required to review the results.

FINAL MSR DOCUMENT

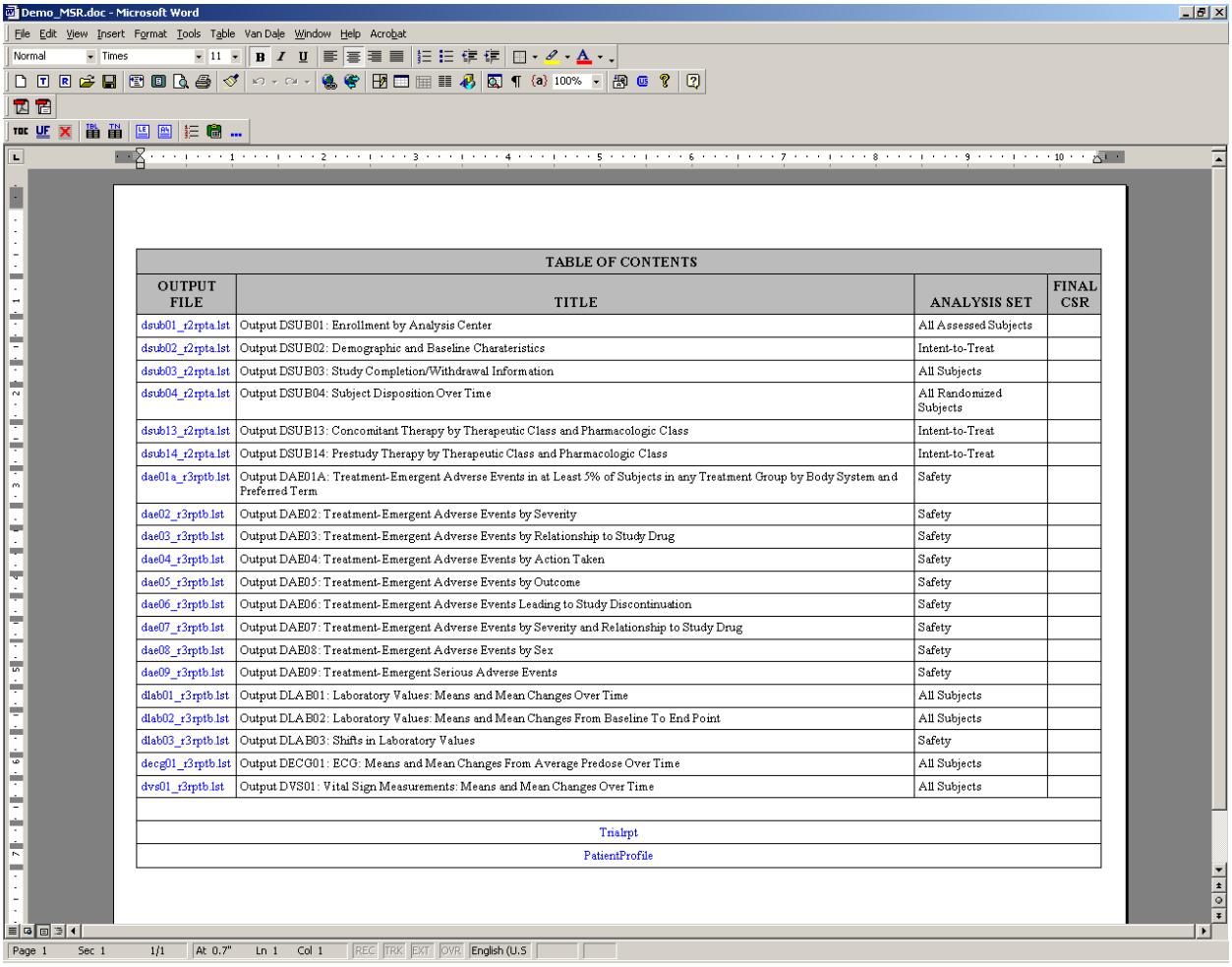
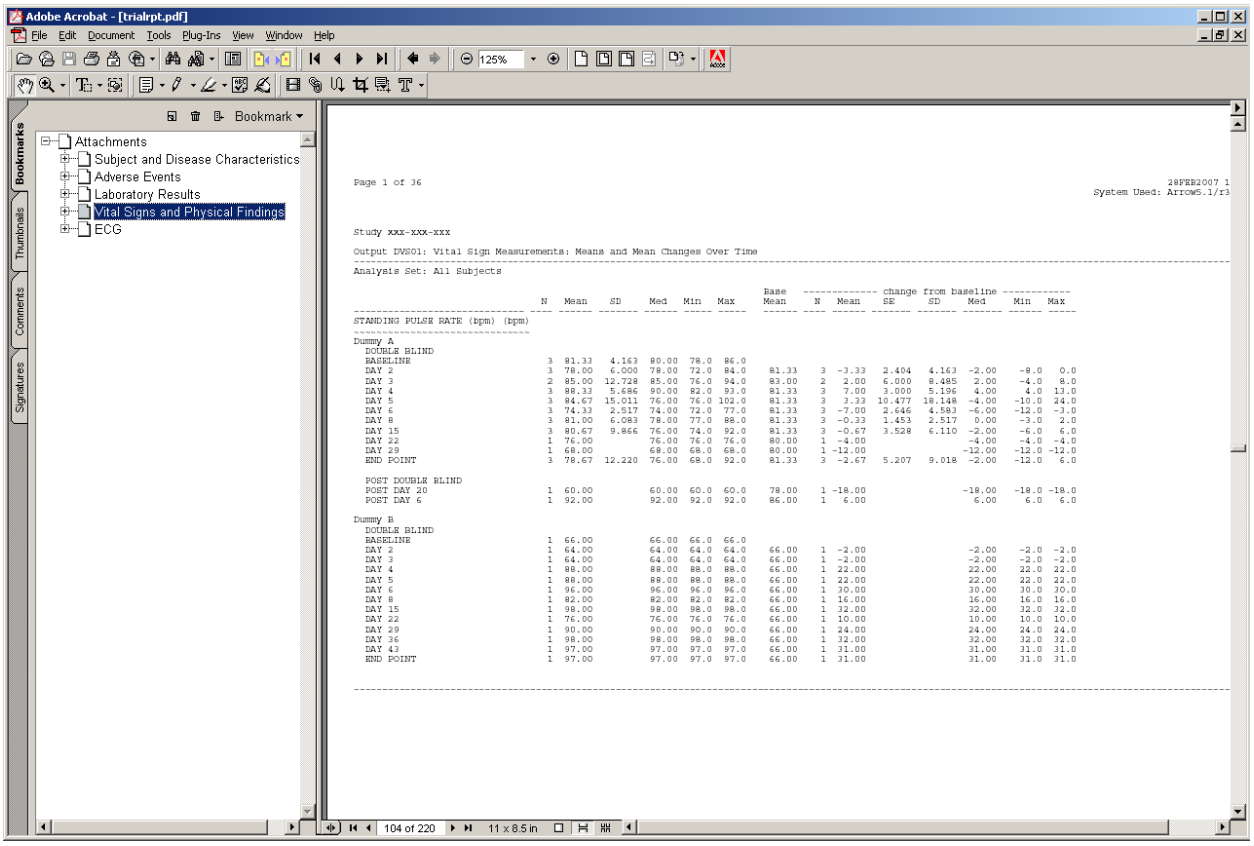


TABLE OF CONTENTS			
OUTPUT FILE	TITLE	ANALYSIS SET	FINAL CSR
dsub01_r2rpta.lst	Output DSUB01: Enrollment by Analysis Center	All Assessed Subjects	
dsub02_r2rpta.lst	Output DSUB02: Demographic and Baseline Charateristics	Intent-to-Treat	
dsub03_r2rpta.lst	Output DSUB03: Study Completion/Withdrawal Information	All Subjects	
dsub04_r2rpta.lst	Output DSUB04: Subject Disposition Over Time	All Randomized Subjects	
dsub13_r2rpta.lst	Output DSUB13: Concomitant Therapy by Therapeutic Class and Pharmacologic Class	Intent-to-Treat	
dsub14_r2rpta.lst	Output DSUB14: Prestudy Therapy by Therapeutic Class and Pharmacologic Class	Intent-to-Treat	
dae01a_r3rptb.lst	Output DAE01A: Treatment-Emergent Adverse Events in at Least 5% of Subjects in any Treatment Group by Body System and Preferred Term	Safety	
dae02_r3rptb.lst	Output DAE02: Treatment-Emergent Adverse Events by Severity	Safety	
dae03_r3rptb.lst	Output DAE03: Treatment-Emergent Adverse Events by Relationship to Study Drug	Safety	
dae04_r3rptb.lst	Output DAE04: Treatment-Emergent Adverse Events by Action Taken	Safety	
dae05_r3rptb.lst	Output DAE05: Treatment-Emergent Adverse Events by Outcome	Safety	
dae06_r3rptb.lst	Output DAE06: Treatment-Emergent Adverse Events Leading to Study Discontinuation	Safety	
dae07_r3rptb.lst	Output DAE07: Treatment-Emergent Adverse Events by Severity and Relationship to Study Drug	Safety	
dae08_r3rptb.lst	Output DAE08: Treatment-Emergent Adverse Events by Sex	Safety	
dae09_r3rptb.lst	Output DAE09: Treatment-Emergent Serious Adverse Events	Safety	
dlab01_r3rptb.lst	Output DLAB01: Laboratory Values: Means and Mean Changes Over Time	All Subjects	
dlab02_r3rptb.lst	Output DLAB02: Laboratory Values: Means and Mean Changes From Baseline To End Point	All Subjects	
dlab03_r3rptb.lst	Output DLAB03: Shifts in Laboratory Values	Safety	
decg01_r3rptb.lst	Output DECG01: ECG: Means and Mean Changes From Average Predose Over Time	All Subjects	
dvs01_r3rptb.lst	Output DVS01: Vital Sign Measurements: Means and Mean Changes Over Time	All Subjects	
Trialrpt			
PatientProfile			

SAFETY TABLES



Page 1 of 36

28FEB2007 1
System Used: Arrow5.1/r3

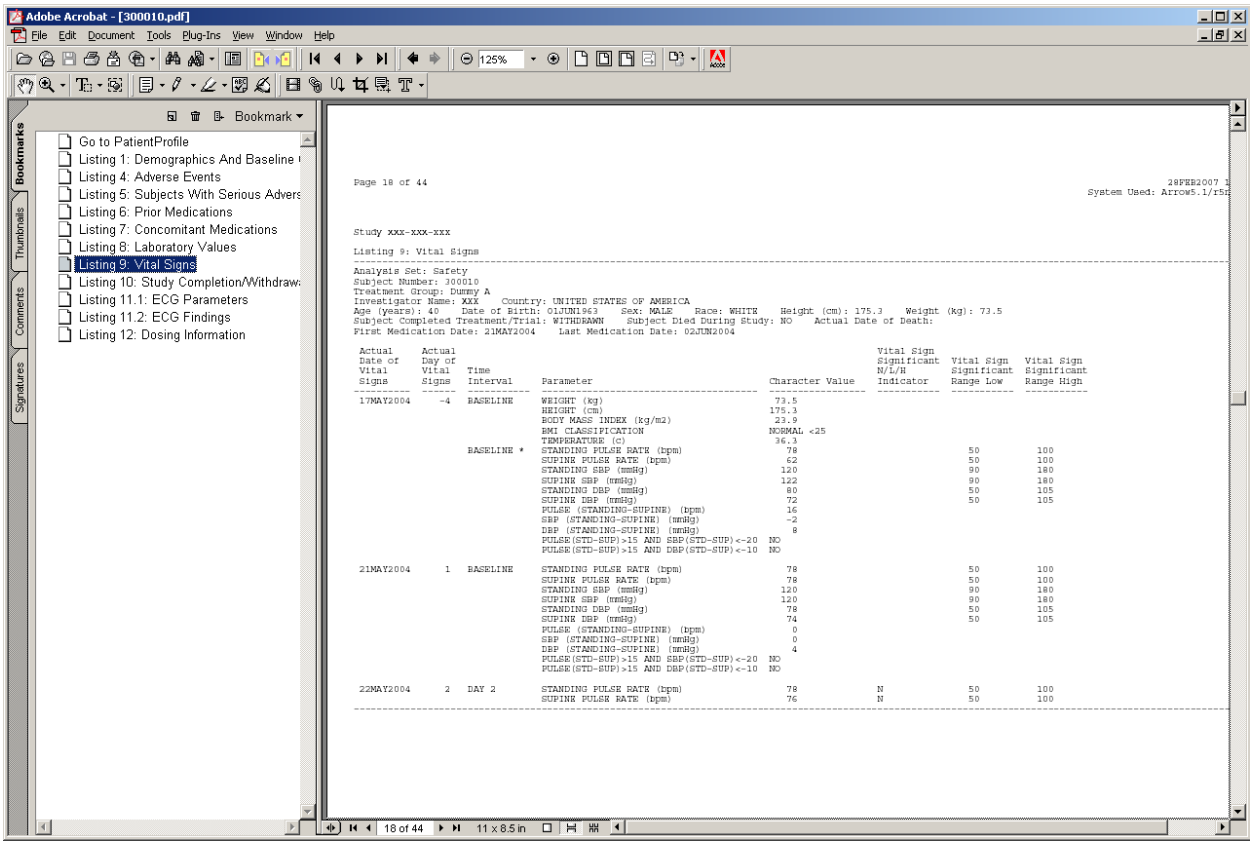
Study xxx-xxx-xxx

Output DVS01: Vital Sign Measurements: Means and Mean Changes Over Time

Analysis Set: All Subjects

	N	Mean	SD	Med	Min	Max	Base Mean	N	change from baseline Mean	SE	SD	Med	Min	Max
STANDING PULSE RATE (bpm) (bpm)														
Dummy A														
DOUBLE BLIND														
BASELINE	3	81.33	4.163	80.00	78.0	86.0								
DAY 2	3	78.00	6.000	78.00	72.0	84.0	81.33	3	-3.33	2.404	4.163	-2.00	-8.0	0.0
DAY 3	2	85.00	12.728	85.00	76.0	94.0	83.00	2	2.00	6.000	8.485	2.00	-4.0	8.0
DAY 4	3	88.33	5.686	90.00	82.0	93.0	81.33	3	7.00	3.000	5.196	4.00	4.0	13.0
DAY 5	3	84.67	15.011	76.00	76.0	102.0	81.33	3	3.33	10.477	18.148	-4.00	-10.0	24.0
DAY 6	3	74.33	2.517	74.00	72.0	77.0	81.33	3	-7.00	2.646	4.583	-6.00	-12.0	-3.0
DAY 8	3	81.00	6.083	78.00	77.0	88.0	81.33	3	-0.33	1.453	2.517	0.00	-3.0	2.0
DAY 15	3	80.67	9.866	76.00	74.0	92.0	81.33	3	-0.67	3.528	6.110	-2.00	-6.0	6.0
DAY 22	1	76.00		76.00	76.0	76.0	80.00	1	-4.00			-4.00	-4.0	-4.0
DAY 29	1	68.00		68.00	68.0	68.0	80.00	1	-12.00			-12.00	-12.0	-12.0
END POINT	3	78.67	12.220	76.00	68.0	92.0	81.33	3	-2.67	5.207	9.018	-2.00	-12.0	6.0
POST DOUBLE BLIND														
POST DAY 20	1	60.00		60.00	60.0	60.0	78.00	1	-18.00			-18.00	-18.0	-18.0
POST DAY 6	1	92.00		92.00	92.0	92.0	86.00	1	6.00			6.00	6.0	6.0
Dummy B														
DOUBLE BLIND														
BASELINE	1	66.00		66.00	66.0	66.0								
DAY 2	1	64.00		64.00	64.0	64.0	66.00	1	-2.00			-2.00	-2.0	-2.0
DAY 3	1	64.00		64.00	64.0	64.0	66.00	1	-2.00			-2.00	-2.0	-2.0
DAY 4	1	88.00		88.00	88.0	88.0	66.00	1	22.00			22.00	22.0	22.0
DAY 5	1	88.00		88.00	88.0	88.0	66.00	1	22.00			22.00	22.0	22.0
DAY 6	1	96.00		96.00	96.0	96.0	66.00	1	30.00			30.00	30.0	30.0
DAY 8	1	82.00		82.00	82.0	82.0	66.00	1	16.00			16.00	16.0	16.0
DAY 15	1	98.00		98.00	98.0	98.0	66.00	1	32.00			32.00	32.0	32.0
DAY 22	1	76.00		76.00	76.0	76.0	66.00	1	10.00			10.00	10.0	10.0
DAY 29	1	90.00		90.00	90.0	90.0	66.00	1	24.00			24.00	24.0	24.0
DAY 36	1	98.00		98.00	98.0	98.0	66.00	1	32.00			32.00	32.0	32.0
DAY 43	1	97.00		97.00	97.0	97.0	66.00	1	31.00			31.00	31.0	31.0
END POINT	1	97.00		97.00	97.0	97.0	66.00	1	31.00			31.00	31.0	31.0

SUBJECT PROFILE LISTING



Page 18 of 44

28FEB2007 1
System Used: Arrow5.1/15

Study xxx-xxx-xxx

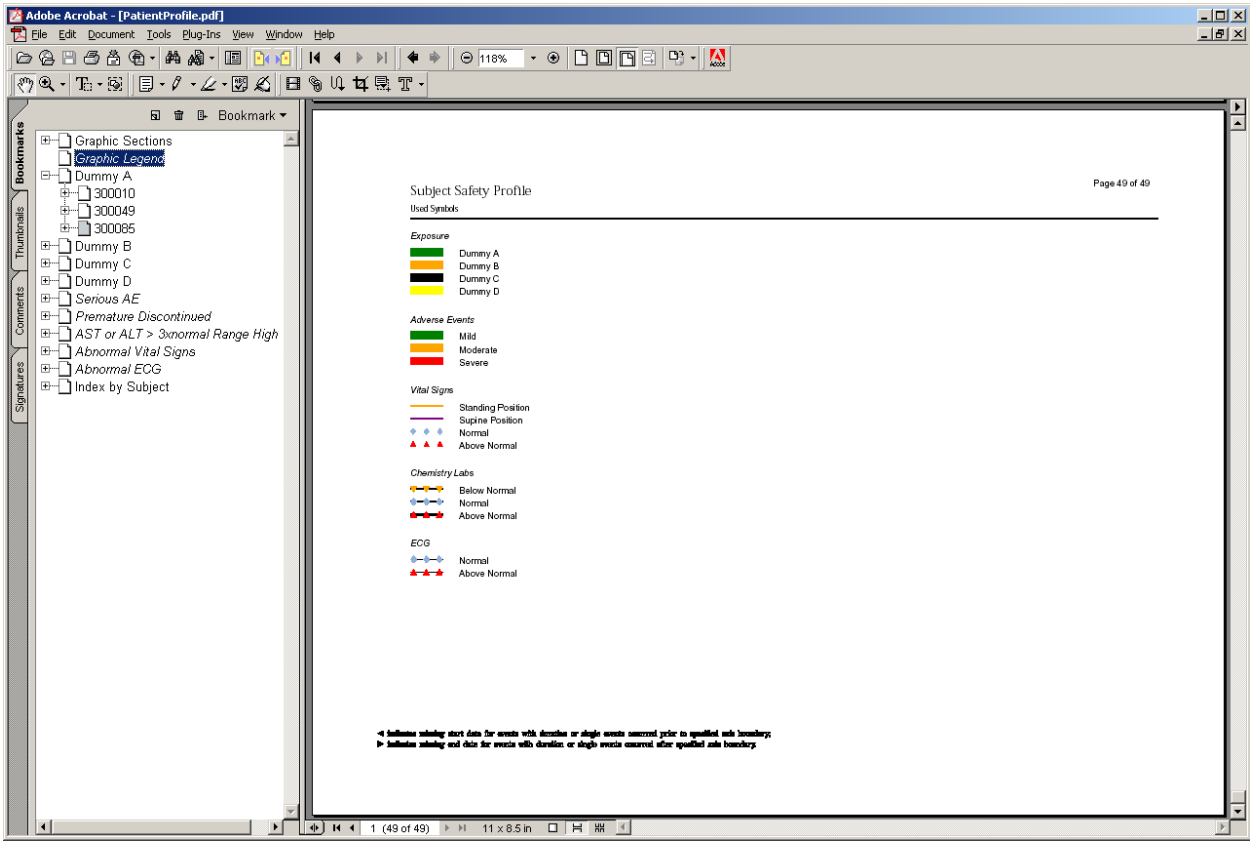
Listing 9: Vital Signs

Analysis Set: Safety
Subject Number: 300010
Treatment Group: Dummy A
Investigator Name: XXX Country: UNITED STATES OF AMERICA
Age (years): 40 Date of Birth: 01JUN1963 Sex: MALE Race: WHITE Height (cm): 175.3 Weight (kg): 73.5
Subject Completed Treatment/Trial: WITHDRAWN Subject Died During Study: NO Actual Date of Death:
First Medication Date: 21MAY2004 Last Medication Date: 02JUN2004

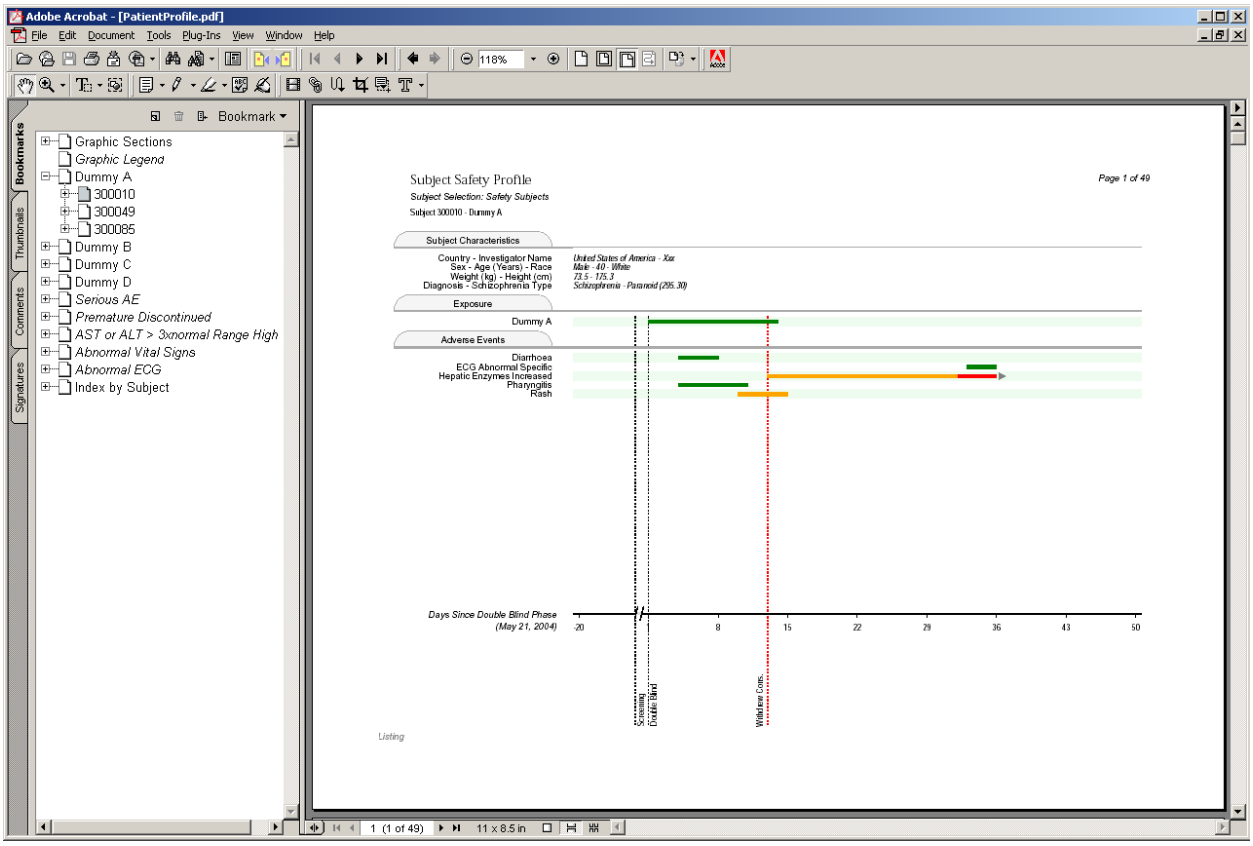
Actual Date of Vital Signs	Actual Day of Vital Signs	Time Interval	Parameter	Character Value	Vital Sign Significant N/L/H Indicator	Vital Sign Significant Range Low	Vital Sign Significant Range High
17MAY2004	-4	BASELINE	WEIGHT (kg)	73.5			
			HEIGHT (cm)	175.3			
			BODY MASS INDEX (kg/m2)	23.9			
			BMI CLASSIFICATION	NORMAL <25			
			TEMPERATURE (C)	36.3			
		BASELINE *	STANDING PULSE RATE (bpm)	78		50	100
			SUPINE PULSE RATE (bpm)	62		50	100
			STANDING SBP (mmHg)	120		90	180
			SUPINE SBP (mmHg)	122		90	180
			STANDING DBP (mmHg)	80		50	105
			SUPINE DBP (mmHg)	72		50	105
			PULSE (STANDING-SUPINE) (bpm)	16			
			SBP (STANDING-SUPINE) (mmHg)	-2			
			DBP (STANDING-SUPINE) (mmHg)	8			
			PULSE(STD-SUP)>15 AND SBP(STD-SUP)<-20	NO			
			PULSE(STD-SUP)>15 AND DBP(STD-SUP)<-10	NO			
21MAY2004	1	BASELINE	STANDING PULSE RATE (bpm)	78		50	100
			SUPINE PULSE RATE (bpm)	78		50	100
			STANDING SBP (mmHg)	120		90	180
			SUPINE SBP (mmHg)	120		90	180
			STANDING DBP (mmHg)	78		50	105
			SUPINE DBP (mmHg)	74		50	105
			PULSE (STANDING-SUPINE) (bpm)	0			
			SBP (STANDING-SUPINE) (mmHg)	0			
			DBP (STANDING-SUPINE) (mmHg)	4			
			PULSE(STD-SUP)>15 AND SBP(STD-SUP)<-20	NO			
			PULSE(STD-SUP)>15 AND DBP(STD-SUP)<-10	NO			
22MAY2004	2	DAY 2	STANDING PULSE RATE (bpm)	78	N	50	100
			SUPINE PULSE RATE (bpm)	76	N	50	100

GRAPHICAL SUBJECT PROFILE

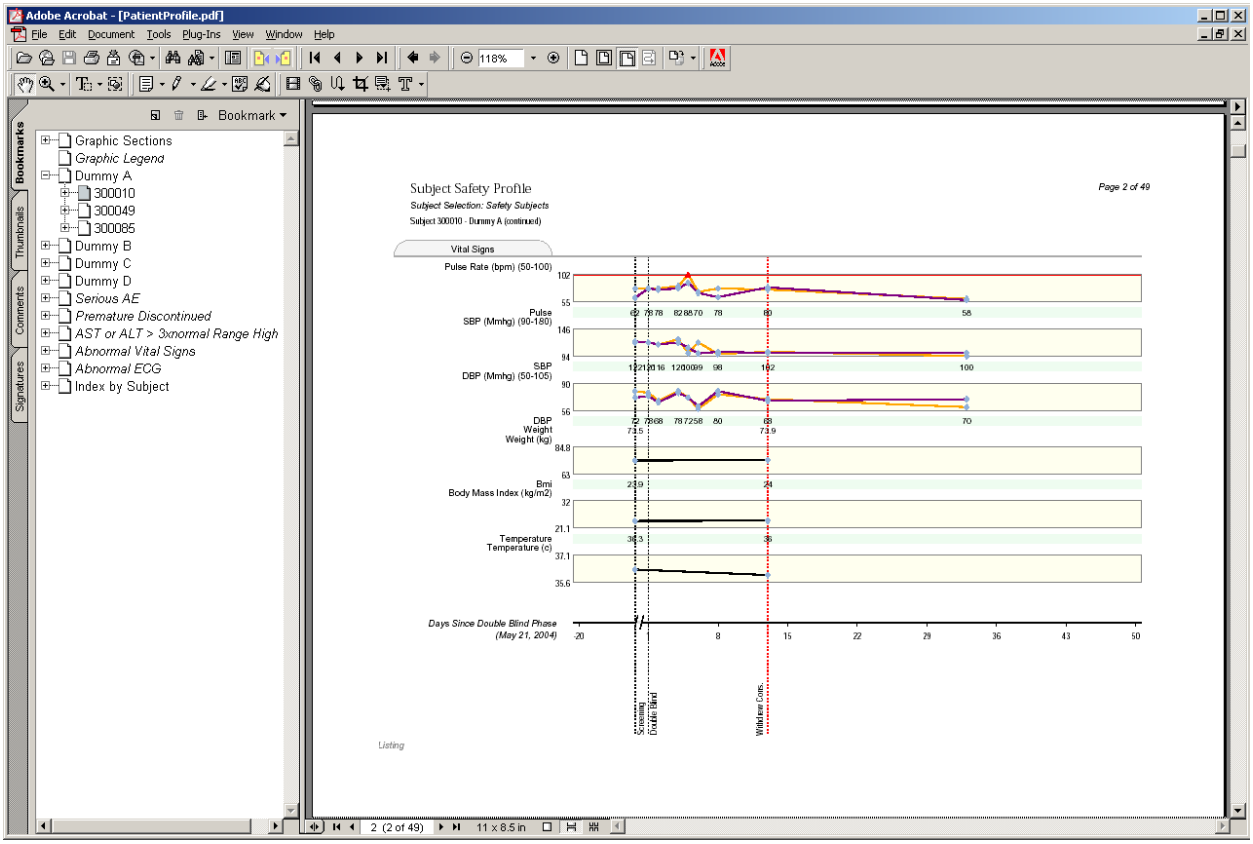
EXAMPLE 1 (LEGEND)



EXAMPLE 2 (SUBJECT CHARACTERISTICS, EXPOSURE AND ADVERSE EVENTS)



EXAMPLE 3 (VITAL SIGNS)



CONCLUSION

The strength of this MSR Process is to share all key information through 1 single document which guides the user through the review flow. It ensures a consistent process and deliverables across teams in a timely fashion.

ACKNOWLEDGEMENTS

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CONTACT INFORMATION

Your comments and questions are valued and encouraged. You can contact us by e-mail:

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