Perform an Eagle Eye Review on Outputs Retrospectively

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16-Apr-2016
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Objective

In the hustle and bustle of things, we send out deliverables to our clients to review, then realize there's a glaring typo or entire sections missing. So the key question here is –

Why, What and How,

to ensure quality in project deliverables? There are actually many ways to do this, and in this session, we want to share with you some tips we've picked up, learnt and practised over the years.

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Agenda

- Aspects of *Getting It Right First Time*
- Intensity of Validation @ Different Levels
- Review of the Data Standardization Outputs
- Review of the Statistical outputs
- Conclusion

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Aspects of *Getting It Right First Time*

- Credibility
- Diversified Opportunities within the Company
- Mastering SME
- Flexible Benefits

- Quality
- Cost Effective
- Leading Indicator of Company's Loyalty
- Time Management

REWORK

- Resource utilization
- Creating your own signature
- Retaining the existing client
- Business growth
- Profit

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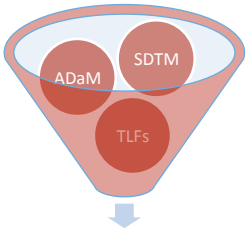
Intensity of Validation @ Different Levels

…Traditional Way of doing..

EAGLE EYE

Validation @ Validator End

- **Verification Checks**
- **Output Validation by secondary coding**
- **Compliance Checks**



Review @ SME End

- **Quality Checks**
- **Traceability**
- **Cross Validation across Outputs**

CLIENT COMMENTS

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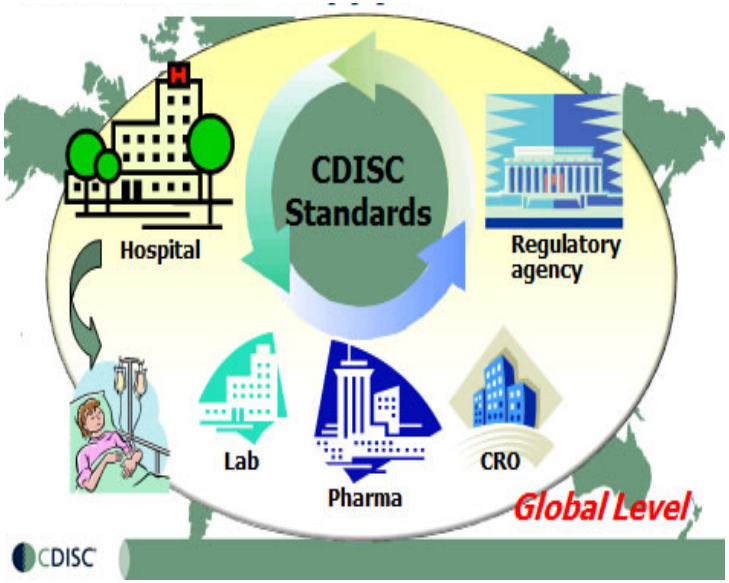
Review of Data Standardization

Study Data Validation

To ensure that the submitted data are both **Compliant** and **Intended** use

- Structure Checks
- Compliance Checks
- Quality Checks
- Study Data Traceability



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Review of Data Standardization

Compliance Checks – To ensure that the data conforms to the standards

Dataset Name	Domain Label Conformance	Mi
DM	Pass	No
DS	Pass	No
EX	Fail	No
QS	Pass	No
SC	Pass	No
SUPPCM	Pass	No
SUPPEX	Pass	No
TA	Pass	No
TE	Pass	No
TI	Pass	No
TS	Pass	No
TV	Pass	No

Rule ID	Message	Description	Category	Type	Example/Explanation
SD0072	Referenced Domain not found	When comments are related to a domain, then the value of Related Domain Abbreviation (RDOMAIN) variable must reference the Domain Code of the parent domain.	Consistency	Error	Occurs for CO when using split domains e.g. QSMM, QSCG. The referenced domain (RDOMAIN = QS) does not exist
SD0074	Referenced Domain not found	Identifies Supplemental Qualifiers domain reference to a key variable that isn't defined in the target domain	Consistency	Error	Occurs for SUPP-- when using split domains e.g. QSMM, QSCG. The referenced domain (RDOMAIN = QS) does not exist
SD0035	Missing units on value	Identifies records that violate the condition [Dose Units is not null], limited to records where [Dose is not null]	Consistency	Error	This error often appears for the Conmeds domain (CM). Cleaning criteria on Conmed questions tend not to be as strict as other domains such as the Study Treatment Exposure (EX). For Conmeds this could be a warning only
SD0013	Begin day must be less than or equal to end day	Begin day must be less than or equal to end day	Limit	Error	This error often appears for the Conmeds domain (CM), where a conmed has a partial start date (CMSTDTC) and a complete end date (CMENDTC).

Variable Having Non-Std Length
ARM
ARMCD
None
None
QSTEST
QSTESTCD
SCTEST
None
None
ARMCD
None
IETEST
None
ARM
ARMCD

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Review of Data Standardization

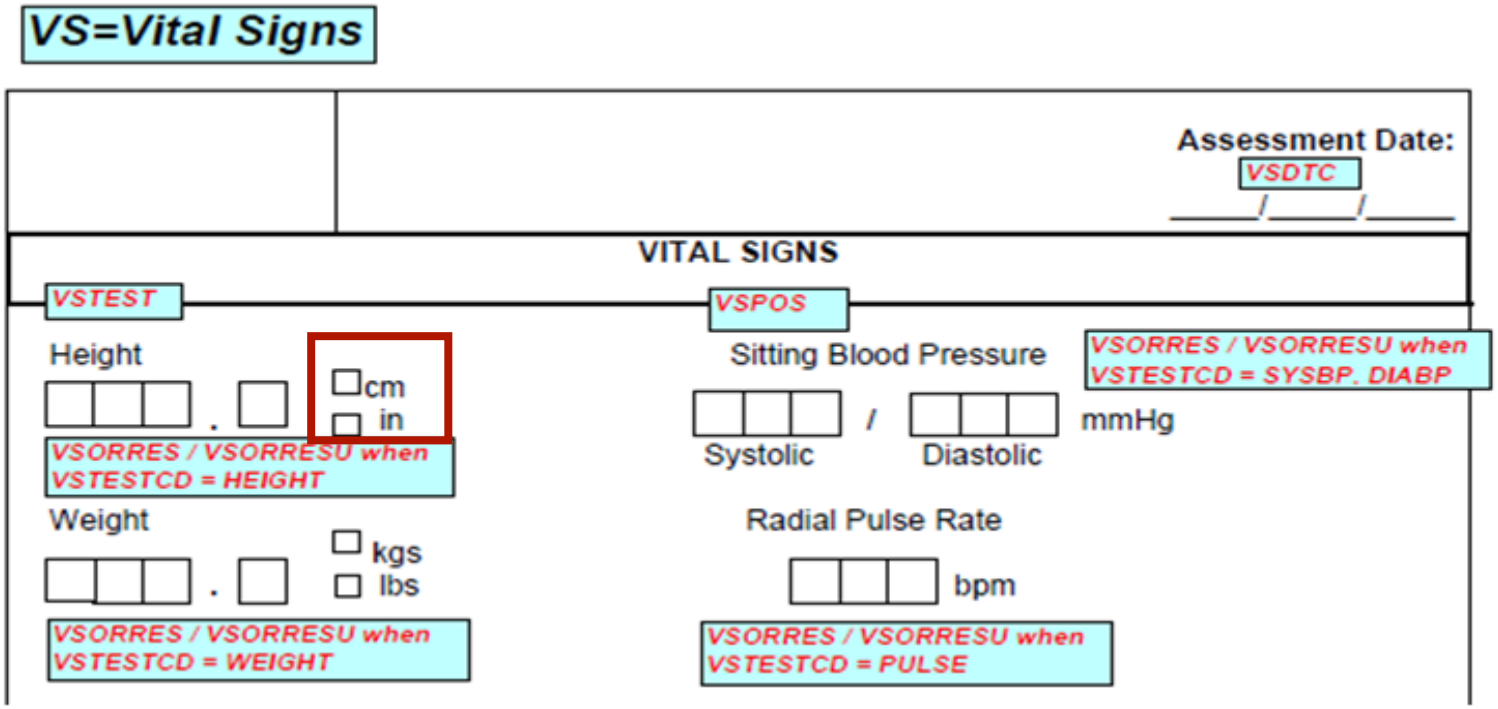
Quality Checks

- CLASS Identification - Deciding between SUPPLEMENTAL QUALIFIERS, FINDINGS and FINDINGS ABOUT
- Custom Domain Assumptions
- Ongoing Vs Legacy Studies
- Not using Standard SUPPQUAL QNAMS
- Adding Duplicate Data
  - Numeric and Character Codes
  - CDISC Controlled Terminology
  - Dates and Times
- Relating Records (RELREC)

Review of Data Standardization

Study Data Traceability - SDTM Dataset vs aCRF

Non-Collected CRF Variables



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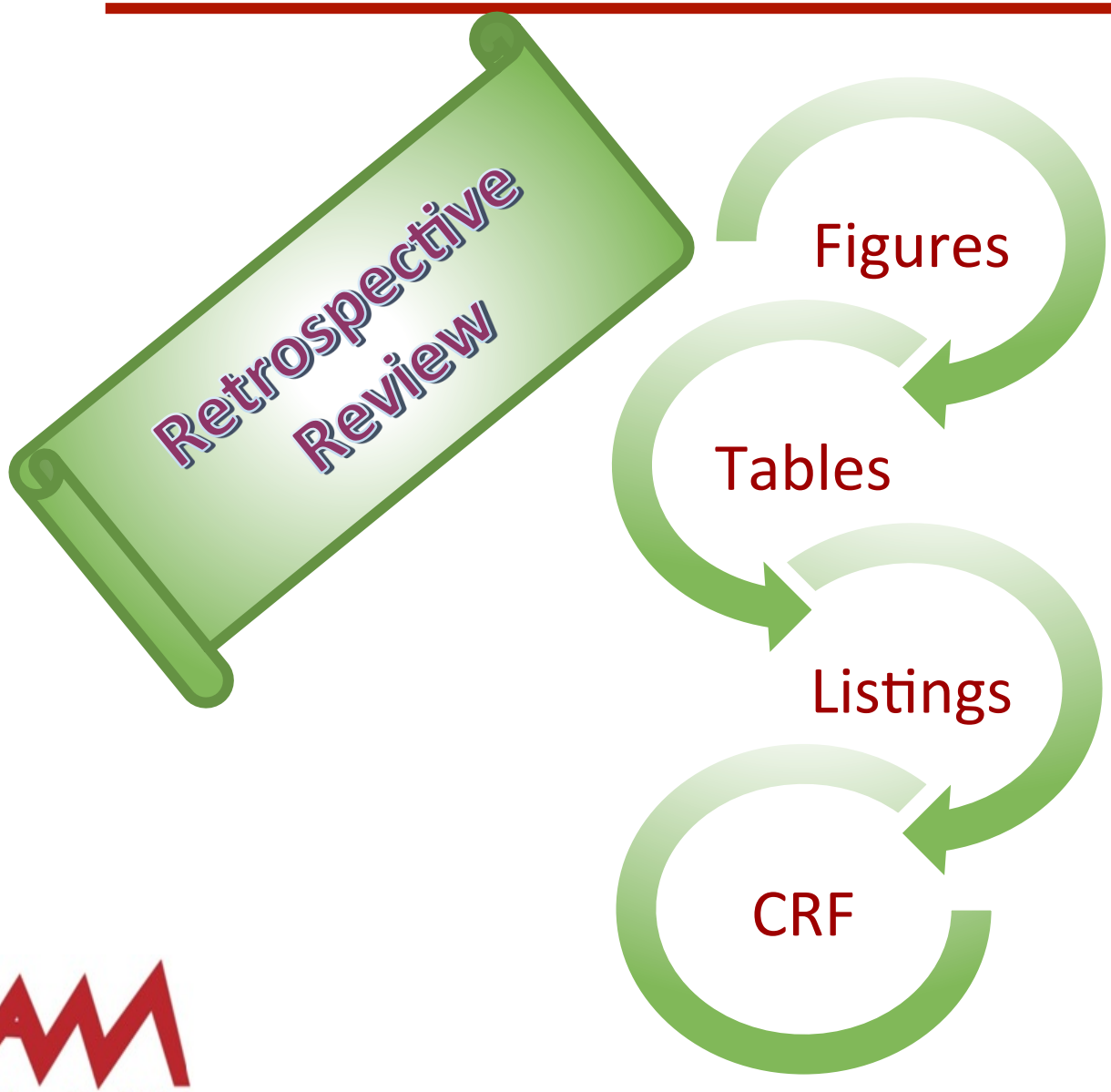
Review of Statistical Outputs



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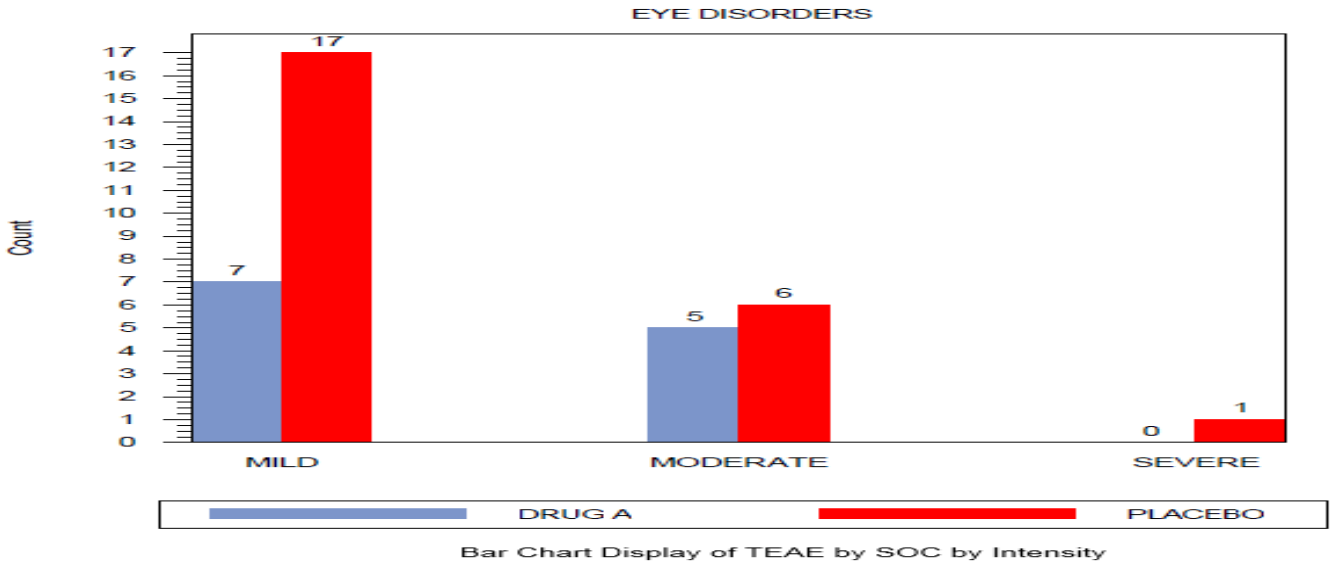
Review of Statistical Outputs

Cross Validation: Figure Vs Table



Bar Chart Display of TEAE by SOC by Intensity

Table 14.3.1.3.1
Incidence of Treatment-Emergent Adverse Events by MedDRA System Organ Class and Maximum Reported Severity
Safety Population

MedDRA System Organ Class	Severity	DRUG A (N=134) n (%)	Placebo (N=152) n (%)	Overall (N=286) n (%)
EYE DISORDERS	MILD	7 (5.2)	17 (11.2)	24 (8.4)
	MODERATE	5 (3.7)	6 (3.9)	11 (3.8)
	SEVERE	0	1 (0.7)	1 (0.3)
GASTROINTESTINAL DISORDERS	MILD	29 (21.6)	32 (21.1)	61 (21.3)
	MODERATE	14 (10.4)	16 (10.5)	30 (10.5)
	SEVERE	2 (1.5)	2 (1.3)	4 (1.4)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	MILD	17 (12.7)	26 (17.1)	43 (15.0)
	MODERATE	12 (9.0)	14 (9.2)	26 (9.1)
	SEVERE	0	2 (1.3)	2 (0.7)

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Review of Statistical Outputs

Cross Validation: Table Vs Tables

xxxx xxx Inc
Protocol xxxx xxx Multicenter

Table 14.3.1.1
Overall Treatment Emergent Adverse Event (TEAE) Summary
Safety Population

Patients with at least one:	Drug A (N=134) n (%)	Placebo (N=152) n (%)	Overall (N=286) n (%)
TEAE	121 (90.3)	135 (88.8)	256 (89.5)
Treatment Related TEAE	67 (50.0)	104 (68.4)	171 (59.8)
Serious TEAE (TESAE)	29 (21.6)	23 (15.1)	52 (18.2)
Treatment-Related TESAE	7 (5.2)	9 (5.9)	16 (5.6)
TEAE Causing Study Drug Discontinuation	9 (6.7)	26 (17.1)	35 (12.2)
Serious TEAE Causing Study Drug Discontinuation	5 (3.7)	3 (2.0)	8 (2.8)

Table 14.3.1.4.2
Incidence of Treatment-Emergent, Treatment-Related Adverse Events by MedDRA System Organ Class and Preferred Term
Safety Population

MedDRA System Organ Class	MedDRA Sy	Drug A	Placebo (N=152) n (%)	Overall (N=286) n (%)
ANY	ANY		104 (68.4)	171 (59.8)
CARDIAC DISORDERS	ANY		2 (1.3)	3 (1.0)
	ANGINA PE		1 (0.7)	1 (0.3)
	ATRIAL FL		1 (0.7)	1 (0.3)
	MYOCARDIA		0	1 (0.3)
EAR AND LABYRINTH DISORDERS	ANY		1 (0.7)	1 (0.3)
	VERTIGO		1 (0.7)	1 (0.3)

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Review of Statistical Outputs

Cross Validation: Table Vs Listing

Listing 16.2.7.3.1
Serious Treatment Emergent Adverse Event
Safety Population

Double-Blind Treatment: PLACEBO

Patient	System Organ Class/ Preferred Term/ Verbatim Term	Severity	Relation	Serious	Action Taken	Treatment Given	Outcome	Start Date	End Date
1054-5001	PSYCHIATRIC DISORDERS/ PSYCHOTIC DISORDER/ PSYCHOTIC EVENT	3	5	SAE REPORTED. PARENT STOPPED STUDY DRUG AFTER AM DOSE ON 01MAY09 - CALLED STUDY STAFF AFTER EVENT.	2		1	29APR2009	05MAY2009
1055-5003	INFECTIONS AND INFESTATIONS/ WOUND INFECTION STAPHYLOCOCCAL/ WOUND INFECTION-MRSA	3	1	Requires/Prolongs Hospitalization	0	VANCOMYCIN	1	16FEB2008	05MAR2008
	PSYCHIATRIC DISORDERS/ AGGRESSION/ VIOLENT BEHAVIOR	3	2	Requires/Prolongs Hospitalization	2	MEDICATION	1	08NOV2008	10NOV2008
1080-5003	GASTROINTESTINAL DISORDERS/ PANCREATITIS ACUTE/ ACUTE PANCREATITIS	3	2	Requires/Prolongs Hospitalization	2	CT OF ABDOMIN WITH CONTRAST	1	08OCT2008	14OCT2008

Relation to Study Drug: 1 = Not Related 2 = Possibly Related 5 = Probably Related
Severity: 1 = Mild 2 = Moderate 3 = Severe
Action taken: 0 = No Action/ Dose Not Changed 1 = Adjusted/ Interrupted 2 = Drug Withdrawn 3 = Dose Reduced 5 = Unknown
6 = Not Applicable

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Review of Statistical Outputs

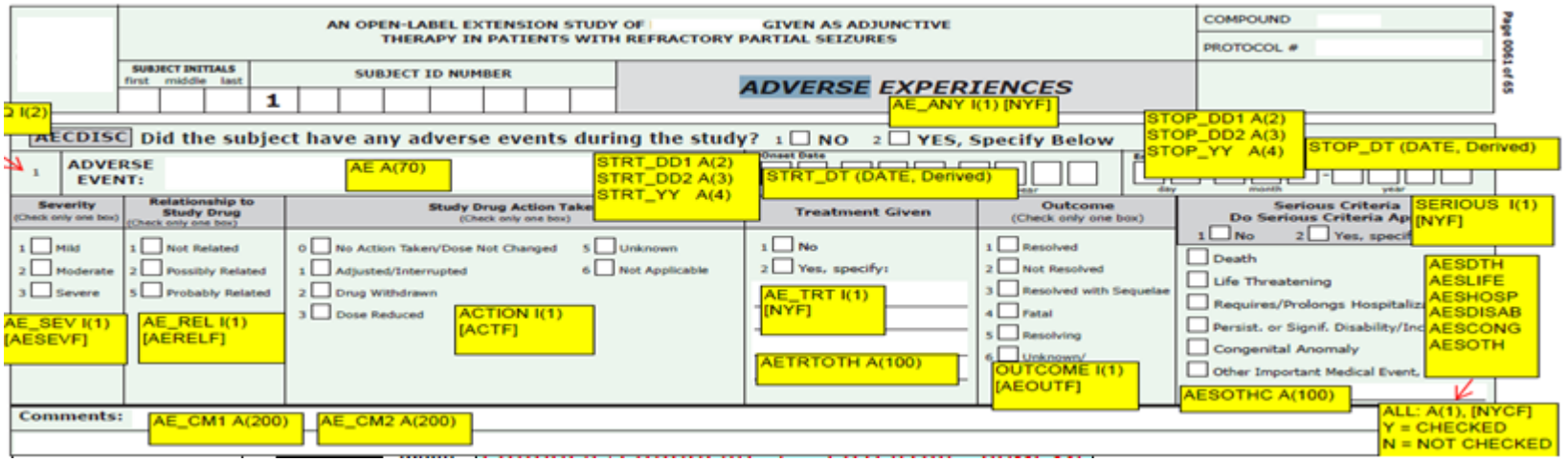
Cross Validation: Listing Vs CRF

Listing 16.2.7.1
Adverse Events
Safety Population

Double-Blind Treatment: PLACEBO

Patient	Dose (mg/day)	System Organ Class/ Preferred Term/ Verbatim Term	Relation	Severity	Action Taken	Treatment Given	Outcome	Start Date	End Date	Duration	Serious
1005-5003	3200	NERVOUS SYSTEM DISORDERS/ EPILEPSY/ HOSPITALIZATION FOR SURGERY DUE TO INTRACTABLE EPILEPSY	1	1	0	GENERAL ANAESTHESIA	1	08JUL2009	17JUL2009	10	Requires/Prolongs Hospitalization

Relation to Study Drug: 1 = Not Related 2 = Possibly Related 5 = Probably Related
Severity: 1 = Mild 2 = Moderate 3 = Severe
Action taken: 0 = No Action/ Dose Not Changed 1 = Adjusted/ Interrupted 2 = Drug Withdrawn 3 = Dose Reduced 5 = Unknown
6 = Not Applicable



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Review of Statistical Outputs

SPOT CHECKS - How to Validate "n" under different scenario

Table 14.1.2
Patient Disposition
Safety Population

	Overall (N=286) n (%)
Completed the study (1)	0
Discontinued from the study	286 (100.0)
Medication non-compliance (study drug or AEDs)	5 (1.7)
Protocol violation	1 (0.3)
Request of the investigator or sponsor	121 (42.3)
Patient withdrew consent	42 (14.7)
Diary non-compliance	1 (0.3)
Adverse experience	35 (12.2)
Other	81 (28.3)
Died during the study (2)	0

- No of subjects randomized =randomization file provided by the statistician
- Completed subjects + Discontinued =Randomized
- No of subjects discontinued =sum (no of subjects under different reasons)
- Number of subjects who have discontinued due to AE= "Any Adverse Event leading to Study Discontinuation"(AE Table)
- Treatment group "N" should not be more than subjects randomized
- Footnote should be relevant

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SPOT CHECKS - How to Validate "n" under different scenario

Table 14.1.3
Demographic and Baseline Characteristics
Safety Population

		DRUG A (N=134)	Placebo (N=152)	Overall (N=286)
Age (years)	n	134	152	286
	Mean (SD)	37.3 (13.95)	37.6 (14.85)	37.5 (14.41)
	Median	36.0	37.0	36.5
	Min, Max	12, 77	13, 75	12, 77
Age group	[12 years, <18 years)	6 (4.5%)	18 (11.8%)	24 (8.4%)
	[18 years, <65 years)	123 (91.8%)	129 (84.9%)	252 (88.1%)
	>=65 years	5 (3.7%)	5 (3.3%)	10 (3.5%)
Sex	Male	71 (53.0%)	72 (47.4%)	143 (50.0%)
	Female	63 (47.0%)	80 (52.6%)	143 (50.0%)
Race	Black	7 (5.2%)	13 (8.6%)	20 (7.0%)
	White	115 (85.8%)	121 (79.6%)	236 (82.5%)
	Hispanic	10 (7.5%)	11 (7.2%)	21 (7.3%)
	Native American	0	2 (1.3%)	2 (0.7%)
	Asian/Pacific Islander	2 (1.5%)	2 (1.3%)	4 (1.4%)
	Other	0	3 (2.0%)	3 (1.0%)
Weight (kg)	n	133	150	283
	Mean (SD)	79.12 (20.506)	78.60 (23.260)	78.84 (21.972)
	Median	77.00	75.50	76.40
	Min, Max	34.5, 134.1	32.7, 140.0	32.7, 140.0

- Check the min, max category with the Inclusion Criteria
- Sum (Sub categories)=N
- Check the categories against the CRF
- Check if the measurements are in same unit
- SD should not be negative

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Conclusion

- Our deliverables are the “face” of our project and they make or break the client’s impression on us.
- So it’s critical that we get our deliverables in top shape.
- A solid quality assurance process is important for ensuring this.
- This additional step and extra effort of review is worth when we get the uncompensated benefit “Quality”.

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Thank You!!!

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