

## TLF Validation Etiquette: What to say, When to Say, How to Say, Why to Say

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### ABSTRACT

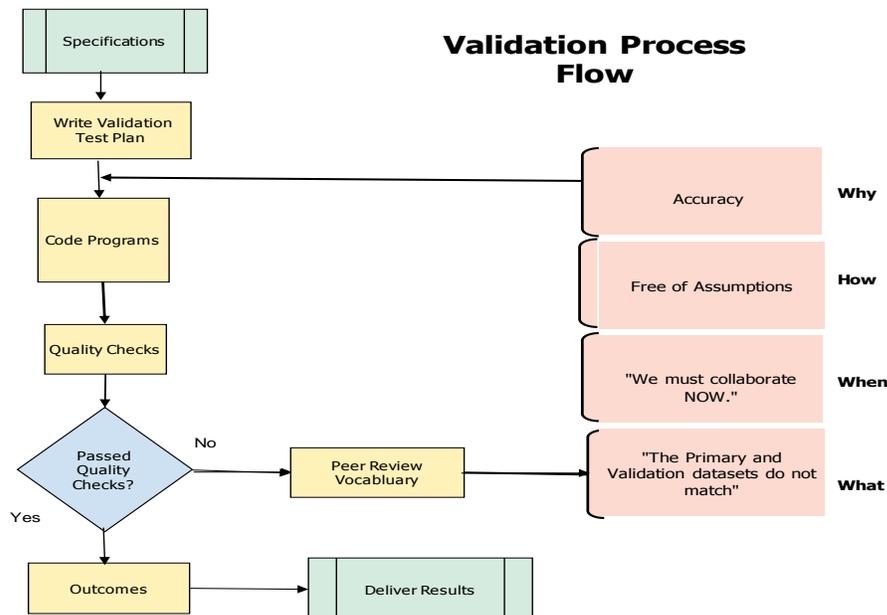
Peer review is the gold standard by where quality is achieved. It has been used to publish scientific journals for centuries. On the internet we see the effects of peer review every day. The peer review process has been mimicked in reality television shows that judge singers, dancers, and even for selecting a spouse. In this paper are the rules by where quality peer review can be done with success and bring forth further insights for SAS programs. Quality is achieved by using a checklist, cooperation, and support. Inherent within this process is the contrast of disparate ideas. That's the beauty of it. Flowing from those disparate ideas; contrast and compared, is proof that one idea is the best suited. Persons involved in this process must agree that the overall quest to discover the best is a collaboration effort. They have to be open to equally capable expertise among one and other, and truly share ideas. Those involved remain free of insult, "bullyism" and "come up isum". Should those latent idiosyncrasies prevail...they will take control. When ego takes over, a programmer and their peer reviewer can find themselves doing everything but collaborating. As a result, the most efficient ideas can be lost to standoff.

### INTRODUCTION

After reading this paper you'll be better equipped to validate SAS programs in the context of peer reviews by using a collection of words and phrases that are safe. This safe vocabulary allows free flowing, and comingling of ideas. Anyone that communicates can learn to master the peer review process and validate a dataset, tables, listings, and figures (TLFs). First we'll use requirement specifications to develop a very important safety report table for subjects using a drug to control blood sugar. We'll then observe the peer review process documenting the validation of the outcomes revealed by the report. As this exercise unfolds, it will demonstrate the best things to say as the process moves along. And will uncover ways to avoid time wasting mistakes that can result in standoff. The Blood Sugar Drug example process is for show only; any similarity to a real study is purely coincidence. This paper aims to begin a new diplomatic "peer reviews" language. Once it catches on, look forward to subsequent accomplishments of wonder for those that use it.

*"It's the ideals we share and the burdens we bare on our collective shoulders to advance them that summons the best in us"...*

President Barack Obama, State of the Union Address, January 2014.



## SPECIFICATIONS

A Development Safety Update Report (DSUR) will do the following: 1) Examine information obtained by a drug sponsor of an investigational drugs safety for a prescribed period. 2) Describe new important safety issues having impact on the clinical trial subject's safety. 3) Summarize their understanding of new risk. 4) Provide an update on the status of the clinical investigation development program and study result. DSUR provides concise information to assure regulation, and that the sponsor is adequately monitoring the evolving safety profile for the investigational drug or ongoing trial.

From the first regulatory approval date up to the date of the last dose of an ongoing study, the DSUR report is due to the FDA every 65 to 75 days, according to the International Conference on Harmonization of Technical Requirements for registration of Pharmaceuticals for Human use. ICH Harmonized Tripartite Guidance Development Safety Update Report E2F, Step. 4 Version (17 August 2010) and EU Commission Guidance Detailed guidance on the Collection, verification, and presentation of adverse events or reaction report arising from clinical trials on medical products for human use.(CT 3)(2011/c 172 01) (11 June 2011).

MedDRA v12.0 Code	CTCAE v4.0 SOC	CTCAE v4.0 Term	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	CTCAE v4.0 AE Term Definition
10021005	Metabolism and nutrition disorders	Hypoglycemia	<LLN - 55 mg/dL; <LLN - 3.0 mmol/L	<55 - 40 mg/dL; <3.0 - 2.2 mmol/L	<40 - 30 mg/dL; <2.2 - 1.7 mmol/L	<30 mg/dL; <1.7 mmol/L; life-threatening consequences; seizures	Death	A disorder characterized by laboratory test results that indicate a low concentration of glucose in the blood.

Figure 1. Common Terminology Criteria for Adverse Events

libname	domemtype	Variable Name	type	length	npos	varnum	label	format	informat	Comment
CDISC	AE DATA	DOMAIN	chr	2	24	1	Domain Abbreviation			
CDISC	AE DATA	USUBJID	chr	200	26	2	Unique Subject Identifier			
CDISC	AE DATA	AEENRF	chr	12	226	3	End Relative to Reference Period			
CDISC	AE DATA	AESER	chr	1	238	4	Serious Event			
CDISC	AE DATA	AESCONG	chr	1	239	5	Congenital Anomaly or Birth Defect			
CDISC	AE DATA	AESDISAB	chr	1	240	6	Persist or Signif Disability/Incapacity			
CDISC	AE DATA	AESDTH	chr	1	241	7	Results in Death			
CDISC	AE DATA	AESHOSP	chr	1	242	8	Requires or Prolongs Hospitalization			
CDISC	AE DATA	AESLIFE	chr	1	243	9	Is Life-Threatening			
CDISC	AE DATA	AESMIE	chr	1	244	10	Other Medically Important Serious Event			
CDISC	AE DATA	AESTDTC	chr	200	245	11	Start Date of Adverse Event			
CDISC	AE DATA	AEENDTC	chr	200	445	12	End Date of Adverse Event			
CDISC	AE DATA	AEOUT	chr	200	645	13	Outcome of Adverse Event			
CDISC	AE DATA	STUDYID	chr	200	645	14	Study Identifier			
CDISC	AE DATA	AESEV	chr	200	1045	15	Severity/Intensity			
CDISC	AE DATA	AEACN	chr	200	1245	16	Action Taken with Study Treatment			
CDISC	AE DATA	AETERM	chr	200	1445	17	Reported Term for the Adverse Event			
CDISC	AE DATA	AEACNOTH	chr	200	1645	18	Other Action Taken			
CDISC	AE DATA	AEREL	chr	200	1845	19	Causality			
CDISC	AE DATA	AEPATT	chr	200	2045	20	Pattern of Adverse Event			
CDISC	AE DATA	AESEO	num	8	0	21	Sequence Number			
CDISC	AE DATA	AEDECOD	chr	200	2245	22	Dictionary-Derived Term			
CDISC	AE DATA	AEBODSYS	chr	200	2445	23	Body System or Organ Class			
CDISC	AE DATA	AESTDY	num	8	8	24	Study Day of Start of Adverse Event			
CDISC	AE DATA	AEENDY	num	8	16	25	Study Day of End of Adverse Event			
CDISC	AE DATA	AESTRF	chr	6	2645	26	Start Relative to Reference Period			

Figure 2. Study Data Tabulation Model for Adverse Events data definition (SDTM)

Using MEDRA dictionary, and study data tabulation for adverse events, we want to count the number of subjects on study that had an event causing seizures or is life threatening. Our DSUR report will document the events that lasted more than 15 minutes and deliver statistics.

### STATISTICAL ANALYSIS PLAN (SAP)

The SAP breaks down the objectives described in the protocol specifications above for the safety report. It translates them to a technical form. The SAP compiles the DSUR report, and adds an analysis table to use for validation.

To meet the protocol objectives, we will count the number of times a subject had an event of Hypoglycemia while taking study drug. Then contrast that count to a group of subjects having an event without taking any study drug.

	<b>Drug 1 N=X</b>	<b>Placebo N=x</b>
Number of Events (%)	xx(xx.x)	xx(xx.x)
Hypoglycemic Episodes	xx	xx
Censored (%)	xx(xx.x)	xx(xx.x)
Median (minutes)	xx.x	xx.x
Hazard Ratio (95% CI)	x.xxx (x.xxx to x.xxx)	
P-Value (log rank)	x.xxxxxx*	

\*P-VALUES ARE UNADJUSTED FOR MULTIPLE DATA LOOKS AND EARLY STUDY TERMINATION

Figure 3. Mock DSUR Table from the SAP

The SAP shows a mock-up of the DSUR report, and gives definition for an analysis dataset “ADAE” that is one “PROC step away” from producing the safety summary report statistics.

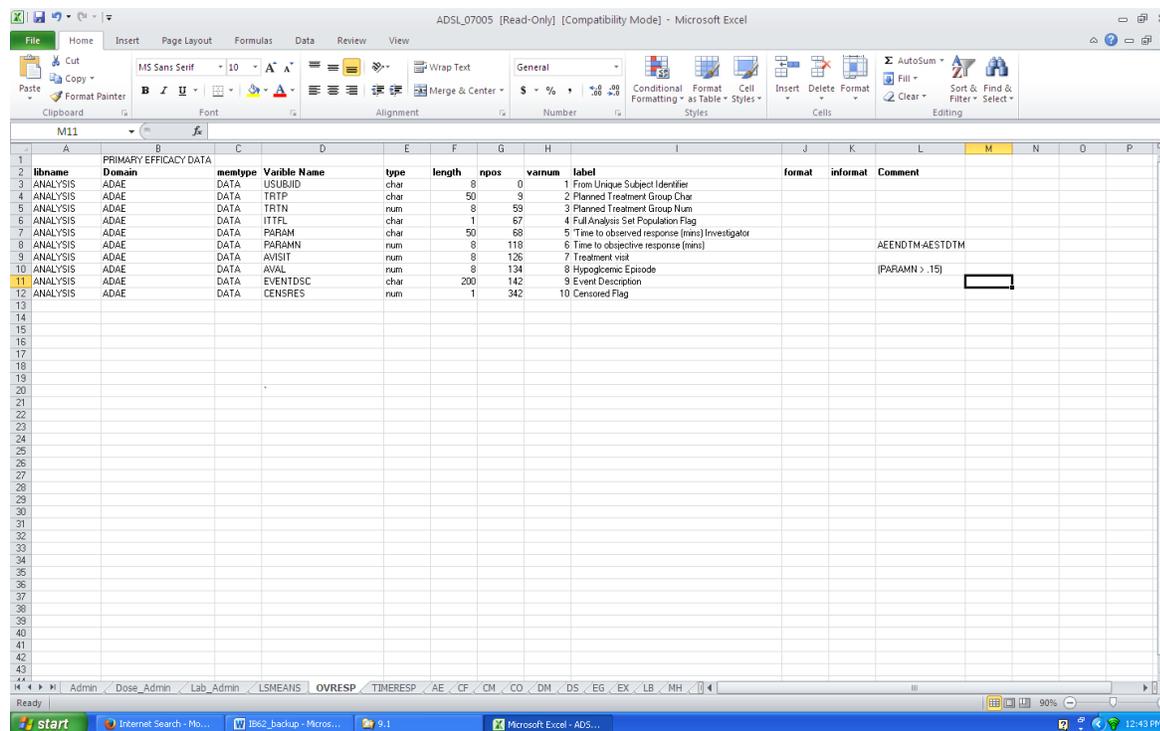


Figure 4. Analysis Table Data Definitions (ADaM)

The SAP will also give the preferred SAS STAT PROC step to summarized the final dataset and capture the calculations.

```
proc phreg data= ADAE
    class TRTP;
    model PARAMN*AVAL(0) = TRTP;
run;
```

## TEST PLAN

For our work today the independent replication level peer review has been prescribed. This kind of quality review requires that both the primary programmer and lead quality validator review the SAP, and develop the same program to produce the “1 off analysis dataset” without looking at each other’s code. Then compare results. Together they develop a test plan and sign off on it to show that essential information has been discussed.

VALIDATION TEST PLAN		DELIVERABLE	ADaM Adverse Event Table
C:/PharmaSUG/2014/TLR/FINAL/ADAE.sas7bdat		PRIMARY PROGRAMMER	Hector
C:/PharmaSUG/2014/TLR/FINAL/Validation/VADAE.sas7bdat		LEAD QUALITY VALIDATOR	Jack
LEVEL	SOURCE DATA PATHNAME	OUTPUT DATA PATHNAME	
Independent Double Blind level 3	C:/PharmaSUG/2014/TLR/SDTM/DATA	C:/PharmaSUG/2014/TLR/Validation/Report	
QUALITY CHECK 1	QUALITY CHECK 2	QUALITY CHECK 3	QUALITY CHECK 4
Frequency Report	Observations: if ITFL=1	Sort key: SUBJID TRT	SAS Proc Compare
NUMBER OF SUBJECTS = 10	SELECTION CRITERIA: AESEV=4	SORT KEYS MATCH ON BOTH	VARIABLE ATTRIBUTES MATCH
Frequency Report	Missing	Merge	SAS Proc Compare
SUBGROUP TRT COUNT	NO MISSING DATA	NO REPEATS OF BY VARIABLES	VALUE CONTENTS MATCH
Pass/Fail	Pass/Fail	Pass/Fail	Pass/Fail
<div style="border: 1px solid black; padding: 5px;"> <p>ADDITIONAL INFORMATION</p> <p>Critical Findings: Please examine and explain any critical findings.</p> </div>			
SIGNATURES:			
PP _____	DATE _____	LQV _____	DATE _____

Figure 5. Sample Validation Test Plan

Essential information includes: the pathnames for the source input, controlled vocabularies, and parameters. The naming conventions followed. The level of validation agreed upon, the location of the SAP, and Protocol documents. The observation counts overall, and for every sub-group, the subject selection, the sort key, the expected number of missing items. Essential information must be exchanged before coding, and is critical to have during the validation peer review process.

The quality validation is proven on the ADAE.sas7bdat dataset. This final dataset will be summarized using the instructions from the SAP. The SAS STAT PROC PHREG has a separate test qualification and its quality has been assured at the time SAS was installed. Doing the quality checks on the final dataset before the stat PROC is sufficient enough. The validation compare table is called VADAE.sas7bdat.

The objective of the test plan is to deliver an ADaM Analysis dataset along with the output report. The names of the peers are included on the test plan. Their validation has been designated level “3”. Most companies have multiple tier levels of validation activities; level 3 is just below the highest. The pathnames of the source data inputs are often computer sub-directories, cabinets, containers, or database instances where all source information is stored.

The test plan describes each quality check in detail. For cases when quality checks don’t cover all critical findings, the peers may add quality checks to the test plan during the validation process. With every cycle of execution of the quality checks, the peers can make updates to them. When critical findings have no quality check, a description of the finding must be documented on the test plan so that it can be addressed. Peers never re-write requirements to accommodate a quality check.

Both peers must sign and date the test plan each time it’s amended. This verifies that each peer has reviewed all proposed quality checks, and shows that a dialog exists between the peers. This open dialog is their way of exchanging ideas, and will help guide them to resolve issues and complete their validation peer review.

## ROLES AND RESPONSIBILITIES

### PRIMARY PROGRAMMER (PP)

The PP is responsible for writing the program that does the work. The PP co-writes the test plan with the LQV. They must agree on all quality checks, exchange and convey essential information. The requirements are never to be changed during the peer review process. The PP executes the final PROC step, formats and writes the report. The PP will add a statement at the end of the primary code that calls the validation program. The PP will review the quality check reports and resolve disagreements between the primary and validation tables. The PP must cooperate with the LQV to resolve critical findings on quality checks.

The PP writes the program "ADAE.SAS" as shown in part below.

```
data ADAE;
  set SDTM.AE;
  attrib
    subjid label='From Unique Subject Identifier'
    TRTP label='Planned Treatment Group char'
    TRTN label='Planned Treatment Group num'
    ITTFL label='Full analysis Set Population Flag'
    PARAM label='Time to objective response'
    PARAMN label='Time to objective response'
    AVISIT label='Treatment Visit number'
    AVAL label='Count of episodes'
    EVENTDSC label='Event Description'
    CENSRES label='Censor Flag'
  ;
  aesttm = input(substr(AESTDTC,12,5),time5.);
  aeentm = input(substr(AEENDTC,12,5),time5.);
  PARAMN = round((aeentm - aesttm)/(60*60),.01);
  AVAL = (PARAMN > .15);
run;
%include VADAE.sas;
```

### LEAD QUALITY VALIDATOR (LQV)

The LQV is responsible for writing the program and verifies the work is accurate. The validation reports double as documented proof that the peer review is complete by showing the tables are matching. The LQV must discuss with the PP the essential information details so the program will read the same source data, and input the "1 off primary table". This is done during the writing of the test plan before coding starts. The LQV must find out if the PP is using a data step style or PROC SQL. Often times, when the PP program is data step the LQV program is done in SQL because that makes for a stronger argument when the data matches. The SAS system must have a valid program qualification (PQ) for PROC SQL. This qualification was done during the system's installation, or during IQ, OQ, PQ. The LQV must cooperate with the PP to resolve critical findings on quality checks.

The LQV writes the validation program "VADAE.SAS" as shown in part below.

```
proc sql;
  create table VADAE
  select subjid, trtp, trtn, ittfll, EVENTDSC, censres, 0 as AVAL,
  int( intck('MINUTES',
  dhms(input(substr(AESTDTC,1,10),yymmdd10.),0,0,input(substr(AESTDTC,12,5),time5.) ) ),
  dhms(input(substr(AEENDTC,1,10),yymmdd10.),0,0,input(substr(AEENDTC,12,5),time5.) ) ) / 60 )
  + .01*
  MOD( intck('MINUTES',
  dhms(input(substr(AESTDTC,1,10),yymmdd10.),0,0,input(substr(AESTDTC,12,5),time5.) ) ),
  dhms(input(substr(AEENDTC,1,10),yymmdd10.),0,0,input(substr(AEENDTC,12,5),time5.) ) ) , 60 ) as
  PARAMN
  from SDTM.AE;
  update VADAE set AVAL = 1 where PARAMN > .15;
quit;

proc compare base=ADAE compare=VADAE
  outnoequal outbase outcomp outdiff listall out=test;
quit;
```

## QUALITY CHECK RESULTS

The quality check reports will be found in the SAS results section Display Manager upon completed execution of the PP program. For our work today we have 4 quality check reports from the test plan that will write to the OUTPUT pane.

### Frequency (Quality Check 1)

A frequency report from “SAS PROC FREQ” will give a count of subjects. There are 10 subjects. Doing a cross frequency report will give a sub-group count by treatment group. There are 2 treatment groups having 5 subjects each in our example. Quality Check 1 has passed.

### Observation Counts / Sub setting/ Selection Criteria (Quality Check 2)

The number of observations is noted on the SAS program log when the SAS program executes. It is 10. During the test plan discussion it is very important for both the PP and LQV to know and agree upon the subject selection criteria. That information is noted in the Protocol and the SAP. From our test plan we see that “if ITTFL=1” means to select the “Intent to Treat” subjects. Subject selection can depend upon randomized list, or it can be as simple as choosing where AESEV=4. All 10 are subjects with severe adverse event. Never allow missing data records to be included in the final analysis set. Quality Check 2 has passed.

### Sub setting / Merging (Quality Check 3)

Data structures for both tables must be the same. The “1 off analysis” table has 1 subject for 1 record of data. During the test plan discussion the PP and LQV must both agree on how the resultant table will be collapsed from a 1 to many SDTM.AE dataset to a 1 to one ADaM.ADAE analysis dataset. The records selected will have a clear and concise definition and it must be noted on the test plan. The sort key for the table must be discussed and agreed upon. This is required for the PROC COMPARE quality check. Having the correct data structure sorted using the same key will result in a clear match between PP and LQV tables. Selecting a different set of subjects or a fuzzy merge will never match. Without conveyance of this essential information the peer review will be a waste time and can be lost to standoff. Quality Check 3 has passed.

### PROC COMPARE (Quality Check 4)

The LQV executed the PROC COMPARE with option METHOD=EXACT for an exact match between the datasets. The PP program generates both datasets upon execution of “%include VADAE.SAS” at the end of primary program “ADAE.SAS”. As thus, the time stamps on them are within seconds. Number of variables (NVar) should match as well as the number of observations (NObs).

```
The SAS System

          The COMPARE Procedure
    Comparison of WORK.ADAE with WORK.VADAE
      (Method=EXACT)

      Data Set Summary

Dataset          Created          Modified  NVar   NObs
WORK.ADAE        10APR14:19:09:17  10APR14:19:09:17    8     10
WORK.VADAE       10APR14:19:09:17  10APR14:19:09:17    8     10

      Variables Summary

Number of Variables in Common: 8.
```

Number of variables in common are 8, and Number of observations read are 10 proves that the first part of Quality Check 4 “Variable Attributes Equal” has passed.

The COMPARE Procedure  
 Comparison of WORK.ADAE with WORK.VADAE  
 (Method=EXACT)

Variables with Unequal Values

Variable	Type	Len	Ndif	MaxDif
PARAMN	NUM	8	6	0.130
AVAL	NUM	8	1	1.000

Value Comparison Results for Variables

Obs		Base PARAMN	Compare PARAMN	Diff.	% Diff
3		0.2500	0.1500	-0.1000	-40.0000
4		1.2500	1.1500	-0.1000	-8.0000
5		0.3300	0.2000	-0.1300	-39.3939
6		0.0500	0.0300	-0.0200	-40.0000
7		0.0500	0.0300	-0.0200	-40.0000
8		0.0800	0.0500	-0.0300	-37.5000

Obs		Base AVAL	Compare AVAL	Diff.	% Diff
3		1.0000	0	-1.0000	-100.0000

The “Obs” column corresponds to the row on both datasets ADAE, and VADAE. The “Base PARAMN” is the value found on ADAE, while the “Compare PARAMN” is the value found on the VADAE. As for values comparisons, PROC COMPARE reports differences starting with the third observations.

Here’s what to do when the value report is not matching:

1. Verify the observation count, subject selection, and sort key on both tables
2. Check variable attributes on the variables having the mismatch on both tables
3. Check that rounding and significant digits are the same for both tables.

This part of Quality Check 4 has failed, as thus all of Quality Check 4 has failed. The programming team must resolve the mismatch. This is a critical finding.

**CRITICAL FINDINGS**

The primary table as it stands now will produce and report one adverse event for the study drug.

	<b>Drug 1 N=5</b>	<b>Placebo N=5</b>
Number of Events (%)	1(20.0)	4(80.0)
Hypoglycemic Episodes	1	4
Censored (%)	5(50.0)	5(50.0)
Median (minutes)	0.076	0.726
Hazard Ratio (95% CI)	5.778 (3.528 to 8.028)	
P-Value (log rank)	0.0790*	

\*P-VALUES ARE UNADJUSTED FOR MULTIPLE DATA LOOKS AND EARLY STUDY TERMINATION

**Figure 6. Development Safety Update Report (DSUR)**

**WHAT TO SAY**

When doing a peer review, it's more efficient to speak in terms of objects rather than 1<sup>st</sup> person. For instance, the LQV will say to the PP *"the primary table and validation tables do not match."* Rather than saying *"Your program is not correct, fix it."* This statement will not come as a surprised, yet still the LQV has to engage and assist the PP by making that statement. Although the next move is on the PP, should it not be made, the LQV will need to motivate the PP by making another statement. *"We have a critical finding on Quality Check 4 that must be resolved before we can proceed"*. If there is still no response the LQV must say *"We have a critical finding at observation 3, how can I help?"*

The next logical thing to do for the PP is review the test plan. The PP will then review the PROC compare results for Quality Check 4 and notice the value mismatch. The PP is subsequently directed to observe both analysis tables.

	SUBJID	PARAMN	AVAL		PARAMN	AVAL
Placebo	101	1	1		1	1
Placebo	102	1	1		1	1
Placebo	104	1.25	1		1.15	1
Placebo	105	0.33	1		0.2	1
Placebo	106	0.05	0		0.03	0
Drug 1	107	0.05	0		0.03	0
Drug 1	108	0.08	0		0.05	0
Drug 1	109	0	0		0	0
Drug 1	110	0	0		0	0
Drug 1	103	0.25	1		0.15	0

In this instance the PP program is not producing the same results as the LQV. The PP and the LQV are equal partners for this peer review. It's the PP's obligation to work with the LQV to make the match happen. The PP must engage and encourage the LQV to change when the PP program is in fact calculating correctly. Both must explore the other's interpretation and logic to make the best choice. Together they will find the best solution for the DSUR at hand.

After matching wits they both see the PP is calculating minutes in terms of percent of an hour, and the LQV is calculating minutes using clock time. They are both correct. The programing dual will need to refer to the test plan to find which will prevail. If nothing found there, they must return to the SAP for the answer to choose one over the other. They find the SAP requires (PARAMN>.15), yet makes no definition for what ".15" is. Perhaps (PARAMN>:15) might have revealed the statistician's intent, but failed syntax? They've exhausted review points from the SAP so they will review the Protocol. They've found a statement in the Protocol specifications that supports the use of "Clock Time" over "Percentage of an hour" time.

Recall... *"Our DSUR report will document the events that lasted more than 15 minutes."*

The PP amends his program code to calculate minutes in terms of clock time. There are no subjects that had an event lasting more than 15 minutes to report on Drug 1. All quality checks must be run again. The inspection of the quality checks shows they have all passed. The DSUR is reported, and verified by a clear validation report.

	Drug 1 N=5	Placebo N=5
Number of Events (%)	0(0.0)	4(80.0)
Hypoglycemic Episodes	0	4
Censored (%)	5(50.0)	5(50.0)
Median (minutes)	0.05	0.68
Hazard Ratio (95% CI)	9.022 (6.792 to 11.252)	
P-Value (log rank)	0.0194*	

\*P-VALUES ARE UNADJUSTED FOR MULTIPLE DATA LOOKS AND EARLY STUDY TERMINATION

**Figure 7. Development Safety Update Report (DSUR)**

## WHEN TO SAY

Safety summaries like the one in our example are usually due hours after an adverse event has occurred. There's no time to waste. The study dosing can be cancelled after 60 days if this report isn't submitted to the FDA in time. The time to say is now. Peers must maintain a close and constant vigil from the beginning until all quality checks have passed. This is accomplished using every utility available: calling on the phone, instant messaging, e-mail, WebEx, join me, share my pc and those alike.

Many of us work from home through computer lines over the VPN. This is a great advantage because we have redefined our work day. The old 9 to 5 standard is obsolete. If it's doable for peers to work constantly on a development safety update report, then it's important enough to go ahead and do it. For those of us who work in the office, we can use the computer utilities, and also we can visit face to face with peers.

For instant messenger, both peers should be signed in and registered with the same IM utility software. Many IM utilities on the internet can be downloaded and customized to suit the needs of the team. For example, use the audio facilities to chime or ring a peer when re-running quality checks.

## HOW TO SAY

Keep in mind that avoiding the mistakes that waste time is adding efficiency to the process. Expect that when done right, a peer review will help add accuracy and confidence to outcomes. Avoid remarks that add nothing to the peer review. The faster ideas are comingled the quicker great outcomes are revealed.

Dos	Don'ts
Spring in to action	Assume
Be honest	Intimidate
Take initiative	Wait
Be respectful	Belittle
Think things through before speaking	Be afraid of silence
Respond to every question	Boast credentials
Review and reflect	Throw over the fence
Be ready available	Miss a call, or IM

## Time wasters

Profiling is so natural to do, we categorized and classify ourselves and others based on little true information. This obstructs listening, and undermines our understanding of each other. Profiling is the opposite of comingling ideas. Where profiling exists miscommunications follow. This will stop peers from reaching a solution. Sometimes a peer can acquiesce to pass failed quality checks because the other peer is perceived to be more credentialed. When peers cannot reach a solution or simply cave in, the peer review is lost to standoff.

When a peer review is lost to standoff, the process can be escalated to add yet a third peer. Although, when this occurs, added time and expense defeats the quality validation effort. An expensive quality validation effort is not sustainable. Unsubstantiated effort without a product attached, and can spiral out of control. Most companies have a standard operating procedure for escalating quality issues.

## WHY TO SAY

If we are to stay in business we'll need to produce accurate reports in a fraction of the time we are doing now. That can be done by working closely with peers comingling ideas during valuation peer review. Just a short time from now we'll need to share ideas across language barriers as we exchange products worldwide. It's useful to have a collection of words and phrases designated and recognized as peer review language. Peer review language conveys and opens exchange that is free of profiling, miscommunication, or standoff. A peer review language with a single focus. That focus is to stay on task until the accuracy of the outcome on a dataset is assured. Communication that's not on task is adding to the expense of the quality review, and making your team less productive in the production of a dataset or TLF.

## CONCLUSION

When developing TLFs, collaborate with peers by building a test plan for quality reviews that is broken down in to quality checks. Comingle ideas and share essential information. Maintain a constant vigil with counterparts using the phone, instant messenger, or other online tools. Be kind and considerate; avoid profiling and other time wasters. If a peer review is lost to standoff escalate using a standard company policy. Know your roles and responsibilities at all times and keep up with peers. When it's time to make a move, do it now. A process that once took 3 weeks can be scaled down to 3 days because we've removed all the extra efforts that are not contributing to the bottom line. The ability to rapidly evolve new compounds and superior outcomes for patients will be achieved proportionally to the extent quality validation efficiency is mastered for biotech companies producing TLFs.

## REFERENCES

Drumy, Bill. April 2014, "In Five Years, Will Pharmaceutical Companies Even Exist?" Pharma Exec's Editorial Advisory Board

## ACKNOWLEDGMENTS

Thanks to all my peer reviews both good and bad that made this paper possible.

## RECOMMENDED READING

- Base SAS® Procedures Guide
- SAS® For Dummies®
- ADaM Implementation Guide
- SDTM Implementation Guide

## CONTACT INFORMATION

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