

Content **U**niformity and **D**issolution **A**cceptance **L**imit Program
Version 2

Users guide

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November 2nd, 2007

BEFORE YOU START:

The program and technical documentation is delivered on a compact disc (CD) AS-IS. Although the author and validation team conducted a validation of the program, there is no warranty as to the programs accuracy or use. Any use of the technical documentation of the information contained therein is at the risk of the user. Documentation may include technical or other inaccuracies or typographical errors.

This SASTM program was written by a statistician and validated by other statisticians from several other pharmaceutical companies. The programs and details of the validation are contained on the CD. Companies may decide to perform additional validation.

In addition to information found in the validation files, the following articles contain details on the method with examples. Note: Methods for content uniformity given in articles prior to the 2007 are not associated with the new USP test. Also, some of the methods used to construct the confidence intervals given in the 1990 paper were revised in subsequent papers.

Bergum, J.S. (1990), *Constructing Acceptance Limits for Multiple Stage Tests*. Drug Development and Industrial Pharmacy, 16(14), 2153-2166.

Bergum, J., Utter, M., *Process Validation* (2000), In: Shein-Chow, ed. Encyclopedia of Biopharmaceutical Statistics, New York: Marcel Dekker, pp 422-439

Bergum, J.S. and Utter M.L. (2003), *Statistical Methods for Uniformity and Dissolution Testing*. *Pharmaceutical Process Validation* edited by Robert A. Nash and Alfred H. Watcher, New York: Marcel Dekker, pp.667-697.

Bergum, J., Li, H. (2007), *Acceptance Limits for the New ICH USP 29 Content Uniformity Test*, *Pharmaceutical Technology*, October, pp 88-98.

OVERVIEW:

The content uniformity and dissolution acceptance limit program (CuDAL) is a set of programs written by James Bergum in SASTM that can be used to evaluate content uniformity and dissolution data against the current USP 29 tests. Process validation and internal release guides are examples of areas where the program has been applied. The program can generate an acceptance limit table for content uniformity and/or dissolution that can be applied to either of two sampling plans. The first sampling plan assumes that one unit is tested for uniformity or dissolution from each of several locations throughout a batch. The second sampling plan assumes that an equal number of units (greater than one) are tested from several locations throughout a batch. For both sampling plans, the user can output the acceptance limit table, perform an evaluation of the table that determines the probability of passing the table given the population parameters, or generate a lower bound on the probability of passing the uniformity or dissolution test for specific sample results. Meeting the acceptance limits given in the table assures that any future sample taken from the batch will pass the corresponding USP 29 content uniformity or dissolution test at least P% of the time with a C% confidence level. The user provides the value of P and C.

The limits constructed and evaluated in these programs are based on the USP 29 tests for dissolution and content uniformity for tablets and capsules (See Appendix for brief descriptions of these tests). Acceptance limits and evaluations can be computed for either content uniformity or dissolution. Since the acceptance limits depend on the sampling plan used, there are four possible choices (2 methods by 2 sampling plans). The two sampling plans are described below:

Sampling Plan 1 assumes one dosage form is tested at each location. So in process validation if one tablet were tested from each of 30 locations, this would follow sampling plan 1. Quality control samples generally are considered to follow sampling plan 1 since samples are taken in short time intervals (ex every 10 minutes) throughout the manufacturing run and composited. So, we assume that a random sample of the composite would result in one dosage form per location. Sampling Plan 2 assumes that more than one dosage form is taken at each location, which is common for process validation. The program assumes that the same number of dosage forms is tested at each location. So, if 4 dosage forms were tested at each of ten different locations during a manufacturing run, this would follow sampling plan 2.

INSTALLATION:

The CD contains the following directories and files:

- Readme File: readme.txt
- Version 2 Users Guide: Users Guide.pdf
- Version 2 Validation Report: Version 2 Validation Report.pdf
- Directory: **V2**
 - SAS Calculation Files:
 - CuDAL.SAS, Cusp1.SAS, Cusp2.SAS, Disp1.SAS, and Disp2.SAS
 - SAS Navigation/Graphical Interface Files: cudal.sas7bcat and files.sas.org
- Directory: **V1**
 - All programs and validation materials for Version 1.

The programs for validation of version 1 are included since the dissolution calculations for version 2 did not change. The validation of the dissolution programs are contained in the V1 documentation. The remainder of this users guide only applies to Version 2.

The SAS™ programs were written in SAS™ Version 8.02 and will run on any IBM or compatible PC that has SAS 8.02 or later on it. The Validation Report contains a validation summary, the signed original protocol, amendments, final amended protocol with signed validation forms, supporting documentation, and validation team curriculum vitas. To navigate the user's guide or validation report, use the navigation pane in Adobe Acrobat Reader. There are also many links that can be used for navigation of these documents. The program can be run directly from the CD (assuming the CD drive is D) or the files can be copied to a PC. If the CD drive is not labeled D, then the file CuDAL.sas must be edited to provide the location of the files in the V2 subdirectory. The CuDAL.sas file is displayed below.

```

***** LIBRARY FOR THE APPLICATION*****;
/* deleting the macro variables */
data vars;
    set sashelp.vmacro;
run;
data _null_;
    set vars;
    if scope='GLOBAL' and name ^= 'SYSODSPATH' then
        call execute('%symdel ' || trim(left(name)) || ';');
run;

libname cudal 'D:\V2';
%global logoloc;
%let logoloc=D:\V2\cudal.jpeg;
options symbolgen mprint mlogic sasautos=('D:\V2');

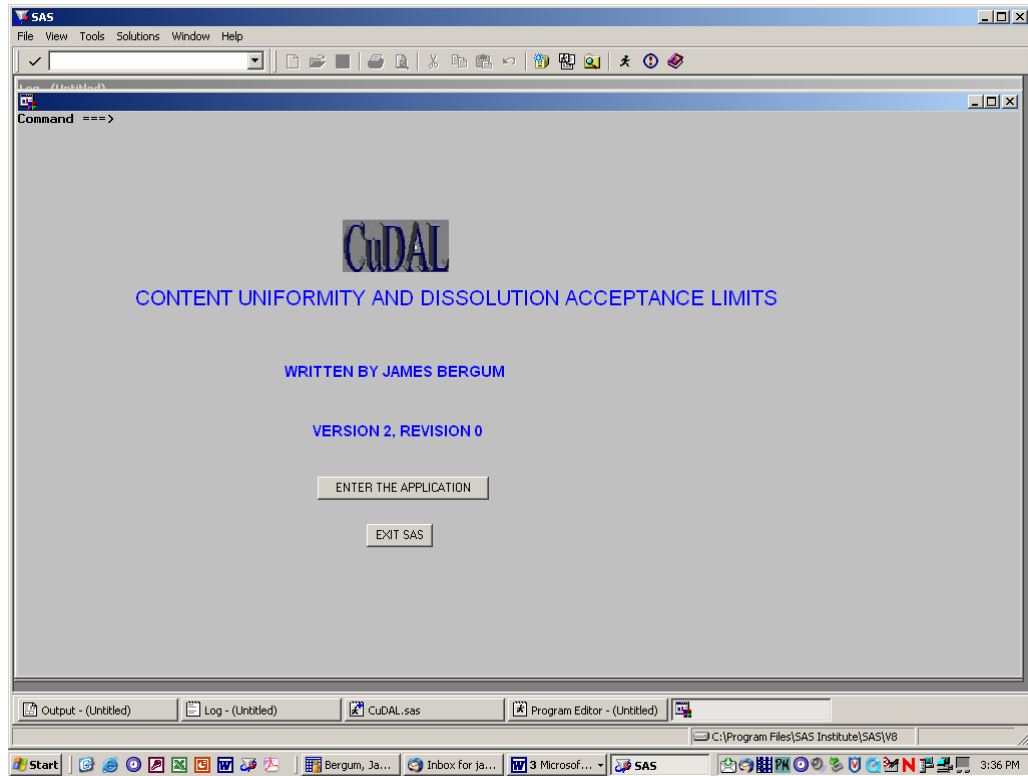
dm 'af c=cudal.cudal.welcome.frame; ' continue;

```

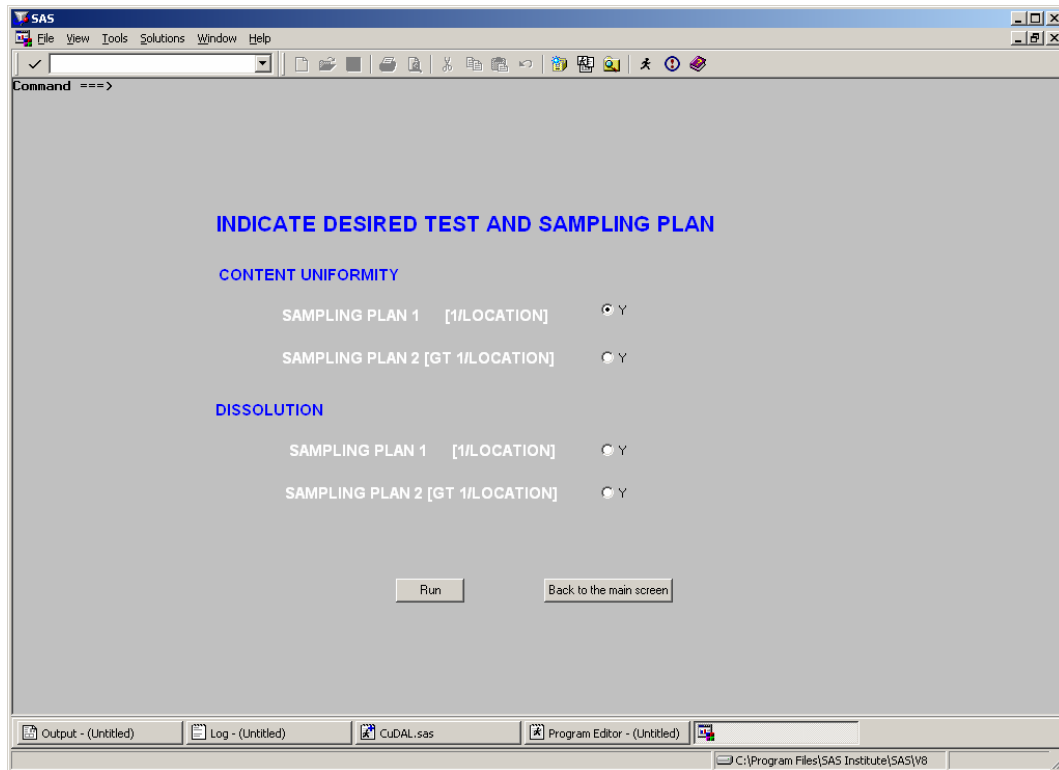
There are three edits required if the program files in the directory V2 are copied from the CD to another location or the drive letter for the CD is not D. Replace **D:\V2** with the appropriate new location. These edits are the only edits required to run the program. No other edits should be made to these programs. [Note: When loading and running the CuDAL program, use a full screen. If the screen is too small, some of the radio buttons may not appear]

USING THE PROGRAM:

To run the program load CuDAL.sas into the SAS™ editor window. After making any necessary edits to the file locations (see above), submit the program. After submitting CuDAL.sas, the following window will appear.



There are two options: Exit SAS or Enter the application. Click on the desired option.
If the option “Enter the Application” is selected, the following test/sampling plan selection screen will appear.



There are four radio buttons that allow the user to select the desired test (content uniformity or dissolution) and sampling plan (one dosage unit per location or multiple dosage units per location). Select the desired button. Depending on the selected button, one of four different windows will appear. Each of these windows and their sub-windows will be discussed separately in the following sections.

Content Uniformity/Sampling Plan 1

If **Content Uniformity/Sampling Plan 1** is selected, the following window appears:

The screenshot shows the SAS window titled "SAS" with a menu bar (File, View, Tools, Solutions, Window, Help) and a toolbar. The main area displays the "CONTENT UNIFORMITY ACCEPTANCE LIMIT PROGRAM FOR SAMPLING PLAN 1 (ONE PER LOCATION)" in yellow text. Below this, there are input fields and radio buttons for the following options:

- ENTER SAMPLE SIZE: 30
- ENTER TARGET: 100
- ENTER BOUND ON FUTURE PERCENTAGE PASSING (50.0-99.0): 95
- ENTER CONFIDENCE LEVEL (50.0-99.0): 95
- DO YOU WANT TO PRINT THE ACCEPTANCE LIMIT TABLE? ☒ Y ☐ N
- DO YOU WANT TO EVALUATE THE ACCEPTANCE LIMIT TABLE? ☐ Y ☒ N
- DO YOU WANT THE LOWER BOUND FOR A SPECIFIC SAMPLE RESULT? ☐ Y ☒ N

At the bottom of the main area are "Run" and "Cancel" buttons. The status bar at the bottom shows the current directory as "C:\Program Files\SAS Institute\SAS\W8". The taskbar at the very bottom shows the Start button, several application icons, and the system clock at 3:43 PM.

The user enters the sample size (i.e., number of dosage units tested), the target (usually average of potency limits (See USP test for more details), the coverage percentage (usually 90 or 95), and the confidence level (usually 90 or 95). There are three choices for SAS output 1) The acceptance limit table, 2) an evaluation of the acceptance limit table, and 3) a calculation of the lower bound based on sample results. The user can pick more than one of these options. The second option calculates the probability of passing the acceptance limit table based on the sample size, coverage, and confidence level selected. The following table appears if this option is selected.

SAS

File View Tools Solutions Window Help

Command ==>

TO EVALUATE LIMITS, THE USER MUST SPECIFY THE RANGE OF POSSIBLE POPULATION VALUES FOR THE MEAN AND CV

ENTER ALL VALUES AS POSITIVE INTEGERS

ENTER LOWER BOUND FOR MEAN: 950

ENTER UPPER BOUND FOR MEAN: 1000

ENTER INCREMENT FOR MEAN: 50

ENTER DIVISOR FOR MEAN: 10

ENTER LOWER BOUND FOR CV: 10

ENTER UPPER BOUND FOR CV: 40

ENTER INCREMENT FOR CV: 30

ENTER DIVISOR FOR CV: 10

Run Cancel

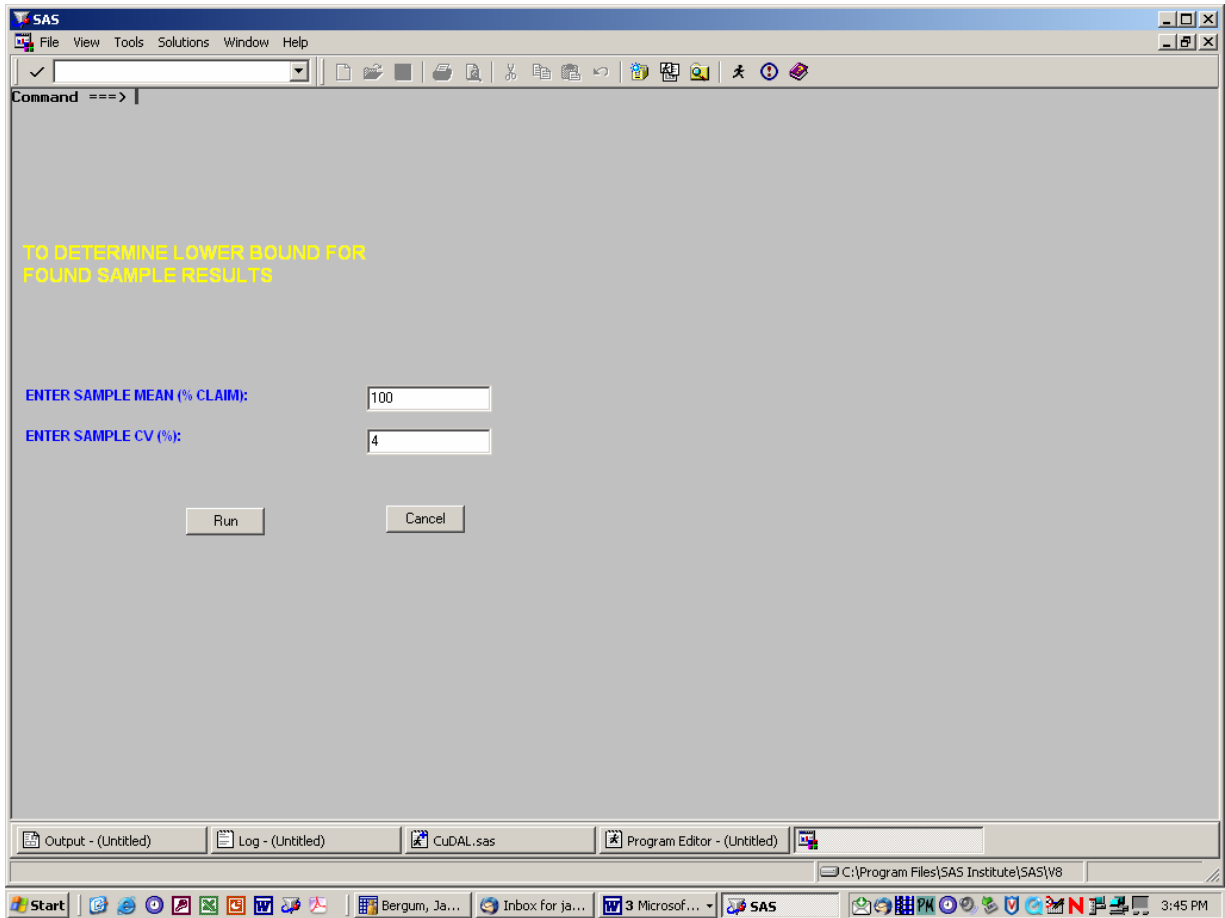
Output - (Untitled) Log - (Untitled) CuDAL.sas Program Editor - (Untitled)

C:\Program Files\SAS Institute\SAS\VB

Start | Bergum, Ja... | Inbox for ja... | 3 Microsof... | SAS | 3:44 PM

The user provides “true” values for the population mean and coefficient of variation (CV) - also called relative standard deviation (RSD) and then using these “true” values, the program calculates the probability that the sample results will fall within the acceptance limits. The entries on this window must all be integers. The lower bound, upper bound, increment, and divisor are entered for both the desired population means and CV’s. The default values indicate that an evaluation is performed using population means of 95.0 and 100.0 and CV’s of 1.0 and 4.0 since the mean goes from 950 to 1000 by 50 and dividing by 10 (i.e., $950/10$, then $1000/10$) and the CV goes from 10 to 40 by 30 (i.e., $10/10$, then $40/10$).

If the 3rd option - **Lower Bound for Sample Result** - is selected, then the following screen appears:



The user enters the sample mean and sample CV.

Sample output from each of these three options are given on the following pages.

ACCEPTANCE LIMITS FOR CONTENT UNIFORMITY(N= 30, TARGET = 100.0)
SAMPLING PLAN 1
(MEETING LIMITS GUARANTEES, WITH 95.0% ASSURANCE, THAT AT LEAST
95.0% OF SAMPLES TESTED FOR CONTENT UNIFORMITY WILL PASS THE USP TEST)

MEAN (% CLAIM)	CV (%)	MEAN (% CLAIM)	CV (%)	MEAN (% CLAIM)	CV (%)	MEAN (% CLAIM)	CV (%)	MEAN (% CLAIM)	CV (%)	MEAN (% CLAIM)	CV (%)
85.1	0.48	90.1	1.87	95.1	3.11	100.1	4.16	105.1	2.76	110.1	1.48
85.2	0.51	90.2	1.89	95.2	3.13	100.2	4.13	105.2	2.73	110.2	1.46
85.3	0.54	90.3	1.92	95.3	3.15	100.3	4.10	105.3	2.71	110.3	1.43
85.4	0.57	90.4	1.94	95.4	3.18	100.4	4.07	105.4	2.68	110.4	1.41
85.5	0.60	90.5	1.97	95.5	3.20	100.5	4.04	105.5	2.65	110.5	1.38
85.6	0.62	90.6	2.00	95.6	3.22	100.6	4.01	105.6	2.63	110.6	1.36
85.7	0.65	90.7	2.02	95.7	3.24	100.7	3.98	105.7	2.60	110.7	1.33
85.8	0.68	90.8	2.05	95.8	3.27	100.8	3.96	105.8	2.58	110.8	1.31
85.9	0.71	90.9	2.07	95.9	3.29	100.9	3.93	105.9	2.55	110.9	1.29
86.0	0.74	91.0	2.10	96.0	3.31	101.0	3.90	106.0	2.52	111.0	1.26
86.1	0.77	91.1	2.13	96.1	3.34	101.1	3.87	106.1	2.50	111.1	1.24
86.2	0.80	91.2	2.15	96.2	3.36	101.2	3.84	106.2	2.47	111.2	1.21
86.3	0.83	91.3	2.18	96.3	3.38	101.3	3.81	106.3	2.44	111.3	1.19
86.4	0.85	91.4	2.20	96.4	3.41	101.4	3.78	106.4	2.42	111.4	1.17
86.5	0.88	91.5	2.23	96.5	3.43	101.5	3.76	106.5	2.39	111.5	1.14
86.6	0.91	91.6	2.25	96.6	3.45	101.6	3.73	106.6	2.36	111.6	1.12
86.7	0.94	91.7	2.28	96.7	3.47	101.7	3.70	106.7	2.34	111.7	1.09
86.8	0.97	91.8	2.30	96.8	3.50	101.8	3.67	106.8	2.31	111.8	1.07
86.9	1.00	91.9	2.33	96.9	3.52	101.9	3.64	106.9	2.29	111.9	1.05
87.0	1.02	92.0	2.35	97.0	3.54	102.0	3.61	107.0	2.26	112.0	1.02
87.1	1.05	92.1	2.38	97.1	3.56	102.1	3.59	107.1	2.24	112.1	1.00
87.2	1.08	92.2	2.40	97.2	3.59	102.2	3.56	107.2	2.21	112.2	0.98
87.3	1.11	92.3	2.43	97.3	3.61	102.3	3.53	107.3	2.18	112.3	0.95
87.4	1.14	92.4	2.45	97.4	3.63	102.4	3.50	107.4	2.16	112.4	0.93
87.5	1.16	92.5	2.48	97.5	3.65	102.5	3.47	107.5	2.13	112.5	0.90
87.6	1.19	92.6	2.50	97.6	3.67	102.6	3.45	107.6	2.11	112.6	0.88
87.7	1.22	92.7	2.53	97.7	3.70	102.7	3.42	107.7	2.08	112.7	0.86
87.8	1.25	92.8	2.55	97.8	3.72	102.8	3.39	107.8	2.06	112.8	0.84
87.9	1.27	92.9	2.58	97.9	3.74	102.9	3.36	107.9	2.03	112.9	0.81
88.0	1.30	93.0	2.60	98.0	3.76	103.0	3.33	108.0	2.00	113.0	0.79
88.1	1.33	93.1	2.63	98.1	3.78	103.1	3.31	108.1	1.98	113.1	0.77
88.2	1.36	93.2	2.65	98.2	3.81	103.2	3.28	108.2	1.95	113.2	0.74
88.3	1.38	93.3	2.68	98.3	3.83	103.3	3.25	108.3	1.93	113.3	0.72
88.4	1.41	93.4	2.70	98.4	3.85	103.4	3.22	108.4	1.90	113.4	0.70
88.5	1.44	93.5	2.72	98.5	3.87	103.5	3.20	108.5	1.88	113.5	0.67
88.6	1.47	93.6	2.75	98.6	3.89	103.6	3.17	108.6	1.85	113.6	0.65
88.7	1.49	93.7	2.77	98.7	3.91	103.7	3.14	108.7	1.83	113.7	0.63
88.8	1.52	93.8	2.80	98.8	3.93	103.8	3.11	108.8	1.80	113.8	0.60
88.9	1.55	93.9	2.82	98.9	3.96	103.9	3.09	108.9	1.78	113.9	0.58
89.0	1.57	94.0	2.84	99.0	3.98	104.0	3.06	109.0	1.75	114.0	0.56
89.1	1.60	94.1	2.87	99.1	4.00	104.1	3.03	109.1	1.73	114.1	0.54
89.2	1.63	94.2	2.89	99.2	4.02	104.2	3.00	109.2	1.70	114.2	0.51
89.3	1.65	94.3	2.92	99.3	4.04	104.3	2.98	109.3	1.68	114.3	0.49
89.4	1.68	94.4	2.94	99.4	4.06	104.4	2.95	109.4	1.65	114.4	0.47

ACCEPTANCE LIMITS FOR CONTENT UNIFORMITY(N= 30, TARGET = 100.0)

SAMPLING PLAN 1

(MEETING LIMITS GUARANTEES, WITH 95.0% ASSURANCE, THAT AT LEAST
95.0% OF SAMPLES TESTED FOR CONTENT UNIFORMITY WILL PASS THE USP TEST)

MEAN (% CLAIM)	CV (%)	MEAN (% CLAIM)	CV (%)	MEAN (% CLAIM)	CV (%)	MEAN (% CLAIM)	CV (%)	MEAN (% CLAIM)	CV (%)	MEAN (% CLAIM)	CV (%)
89.5	1.71	94.5	2.96	99.5	4.08	104.5	2.92	109.5	1.63	114.5	0.44
89.6	1.73	94.6	2.99	99.6	4.10	104.6	2.90	109.6	1.60	114.6	0.42
89.7	1.76	94.7	3.01	99.7	4.12	104.7	2.87	109.7	1.58	114.7	0.40
89.8	1.79	94.8	3.03	99.8	4.14	104.8	2.84	109.8	1.55	114.8	0.38
89.9	1.81	94.9	3.06	99.9	4.16	104.9	2.82	109.9	1.53	114.9	0.35
90.0	1.84	95.0	3.08	100.0	4.18	105.0	2.79	110.0	1.50		

ACCEPTANCE LIMIT TABLE FOR CONTENT UNIFORMITY(N= 30)
SAMPLING PLAN 1
DETERMINE PROBABILITY OF PASSING ACCEPTANCE LIMIT TABLE
CONFIDENCE LEVEL = 95.0 AND LOWER BOUND = 95.0

U	CV	PROBABILITY
		OF PASSING
95	1	1.00000
100	1	1.00000
95	4	0.05220
100	4	0.56434

ACCEPTANCE LIMIT TABLE FOR CONTENT UNIFORMITY(N= 30)

SAMPLING PLAN 1

DETERMINE PROBABILITY OF FUTURE SAMPLES PASSING THE USP TEST
WITH 95.0 ASSURANCE FOR GIVEN SAMPLE MEAN AND CV

SAMPLE MEAN (% CLAIM)	SAMPLE STD DEV (% CLAIM)	CV	LOWER BOUND
100	4	4	0.98003

Content Uniformity/Sampling Plan 2

If Content Uniformity/Sampling Plan 2 is selected, the following screen appears:

The screenshot shows the SAS Content Uniformity Acceptance Limit Program for Sampling Plan 2. The window has a title bar with the SAS logo and menu options: File, View, Tools, Solutions, Window, Help. Below the menu bar is a toolbar with various icons. The main area is titled "CONTENT UNIFORMITY ACCEPTANCE LIMIT PROGRAM FOR SAMPLING PLAN 2 [GREATER THEN ONE SAMPLE PER LOCATION]". It contains several input fields and radio button options. The input fields are: "ENTER NUMBER OF LOCATIONS:" with a value of 10, "ENTER NUMBER PER LOCATION:" with a value of 4, "ENTER TARGET:" with a value of 100, "ENTER BOUND ON FUTURE PERCENTAGE PASSING (50.0-99.0):" with a value of 95, and "ENTER CONFIDENCE LEVEL (50.0-99.0):" with a value of 95. There are three radio button options: "DO YOU WANT TO PRINT THE ACCEPTANCE LIMIT TABLE?" with "Y" selected, "DO YOU WANT TO EVALUATE THE ACCEPTANCE LIMIT TABLE?" with "N" selected, and "DO YOU WANT THE LOWER BOUND FOR A SPECIFIC SAMPLE RESULT?" with "N" selected. At the bottom are "Run" and "Cancel" buttons. The status bar at the bottom shows the current directory as C:\Program Files\SAS Institute\SAS\W8 and the time as 3:46 PM.

Command ==>

CONTENT UNIFORMITY ACCEPTANCE LIMIT PROGRAM FOR
SAMPLING PLAN 2 [GREATER THEN ONE SAMPLE PER LOCATION]

ENTER NUMBER OF LOCATIONS: 10

ENTER NUMBER PER LOCATION: 4

ENTER TARGET: 100

ENTER BOUND ON FUTURE PERCENTAGE PASSING (50.0-99.0): 95

ENTER CONFIDENCE LEVEL (50.0-99.0): 95

DO YOU WANT TO PRINT THE ACCEPTANCE LIMIT TABLE? ☒ Y ☐ N

DO YOU WANT TO EVALUATE THE ACCEPTANCE LIMIT TABLE? ☐ Y ☒ N

DO YOU WANT THE LOWER BOUND FOR A SPECIFIC SAMPLE RESULT? ☐ Y ☒ N

Run Cancel

Output - (Untitled) Log - (Untitled) CuDAL.sas Program Editor - (Untitled)

C:\Program Files\SAS Institute\SAS\W8

Start [Icons] Bergum, Ja... Inbox for Ja... 3 Microsoft... SAS [Icons] 3:46 PM

The user enters the number of locations, the number of dosage units per location, target, the coverage probability, and the confidence level. There are three choices for SAS output 1) The acceptance limit table, 2) an evaluation of the acceptance limit table, and 3) a calculation of the lower bound based on sample results. The user can pick more than one of these options. The second option calculates the probability of passing the acceptance limit table based on the sample size, coverage, and confidence level selected. The following table appears if this option is selected.

TO EVALUATE LIMITS, THE USER MUST SPECIFY THE RANGE OF POSSIBLE POPULATION VALUES FOR THE MEAN, WITHIN LOCATION STD DEV AND BETWEEN LOCATION STD DEV

ENTER ALL VALUES AS POSITIVE INTEGERS

ENTER LOWER BOUND FOR MEAN: 950

ENTER UPPER BOUND FOR MEAN: 1000

ENTER INCREMENT FOR MEAN: 50

ENTER DIVISOR FOR MEAN: 10

ENTER LOWER BOUND FOR WITHIN STD DEV: 22

ENTER UPPER BOUND FOR WITHIN STD DEV: 22

ENTER INCREMENT FOR WITHIN STD DEV: 10

ENTER DIVISOR FOR WITHIN STD DEV: 10

ENTER LOWER BOUND FOR BETWEEN STD DEV: 22

ENTER UPPER BOUND FOR BETWEEN STD DEV: 22

ENTER INCREMENT FOR BETWEEN STD DEV: 10

ENTER DIVISOR FOR BETWEEN STD DEV: 10

Run Cancel

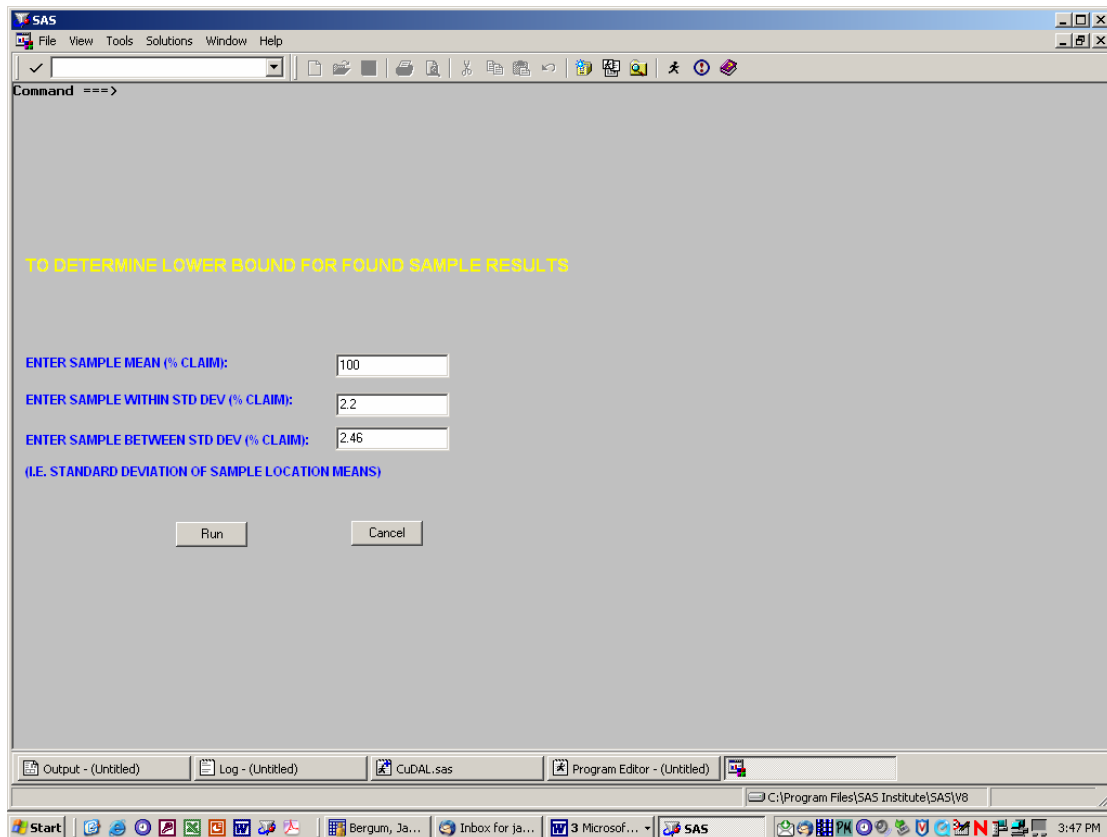
Output - (Untitled) Log - (Untitled) CuDAL.sas Program Editor - (Untitled)

C:\Program Files\SAS Institute\SAS\V8

Start [Icons] 3:47 PM

The user provides “true” values for the population mean, coefficient of variation (CV) within locations, and CV for the between location. Using these “true” values, the program calculates the probability that the sample results will fall within the acceptance limits. The entries on this window must all be integers. The lower bound, upper bound, increment, and divisor are entered for both the desired population means and within/between location CV’s. The default values indicate that an evaluation is performed using population means of 95.0 and 100.0, within location CV of 2.2, and between location CV’ of 2.2 since the mean goes from 950 to 1000 by 50 and dividing by 10 (i.e., $950/10$, then $1000/10$) and the CV’s go from 22 to 22 by 10 (i.e., only one value - $22/10$).

If the 3rd option - **Lower Bound for Sample Result** - is selected, then the following screen appears:



The user enters the sample mean, within sample standard deviation, and between sample standard deviation [Note: This is just the sample standard deviation of the sample means, not a variance component!]

Sample output from each of these three options are given on the following pages.

ACCEPTANCE LIMITS FOR CONTENT UNIFORMITY
SAMPLING PLAN 2
TARGET=100.0, LOWER BOUND = 95.0, CONFIDENCE LEVEL = 95.0
TABLE ENTRIES ARE LOWER(LL) AND UPPER(UL) LIMITS ON THE MEAN
OF 40 ASSAYS- 4 ASSAYS AT EACH OF 10 DIFFERENT LOCATIONS
SE IS THE POOLED WITHIN LOCATION STANDARD DEVIATION
STANDARD DEVIATIONS AND MEANS ARE EXPRESSED IN % CLAIM

STANDARD DEVIATION OF LOCATION MEANS

	0.1		0.2		0.3		0.4		0.5		0.6		0.7		0.8		0.9	
SE	LL	UL	LL	UL	LL	UL	LL	UL	LL	UL	LL	UL	LL	UL	LL	UL	LL	UL
0.1	84.8	115.2	84.8	115.2	85.3	114.7	85.9	114.1	86.5	113.5	87.1	112.9	87.7	112.3	88.3	111.7	88.8	111.2
0.2	84.7	115.3	84.8	115.2	85.4	114.6	86.0	114.0	86.5	113.5	87.1	112.9	87.7	112.3	88.3	111.7	88.9	111.1
0.3	84.6	115.4	85.0	115.0	85.5	114.5	86.0	114.0	86.6	113.4	87.2	112.8	87.7	112.3	88.3	111.7	88.9	111.1
0.4	84.9	115.1	85.2	114.8	85.6	114.4	86.1	113.9	86.7	113.3	87.2	112.8	87.8	112.2	88.4	111.6	88.9	111.1
0.5	85.2	114.8	85.4	114.6	85.8	114.2	86.2	113.8	86.8	113.2	87.3	112.7	87.8	112.2	88.4	111.6	89.0	111.0
0.6	85.4	114.6	85.7	114.3	86.0	114.0	86.4	113.6	86.9	113.1	87.4	112.6	87.9	112.1	88.5	111.5	89.0	111.0
0.7	85.7	114.3	85.9	114.1	86.2	113.8	86.6	113.4	87.0	113.0	87.5	112.5	88.0	112.0	88.6	111.4	89.1	110.9
0.8	86.0	114.0	86.2	113.8	86.5	113.5	86.8	113.2	87.2	112.8	87.7	112.3	88.2	111.8	88.7	111.3	89.2	110.8
0.9	86.3	113.7	86.5	113.5	86.7	113.3	87.0	113.0	87.4	112.6	87.8	112.2	88.3	111.7	88.8	111.2	89.3	110.7
1.0	86.6	113.4	86.8	113.2	87.0	113.0	87.3	112.7	87.6	112.4	88.0	112.0	88.4	111.6	88.9	111.1	89.4	110.6
1.1	86.9	113.1	87.1	112.9	87.3	112.7	87.5	112.5	87.8	112.2	88.2	111.8	88.6	111.4	89.1	110.9	89.6	110.4
1.2	87.2	112.8	87.3	112.7	87.5	112.5	87.8	112.2	88.1	111.9	88.4	111.6	88.8	111.2	89.2	110.8	89.7	110.3
1.3	87.5	112.5	87.6	112.4	87.8	112.2	88.0	112.0	88.3	111.7	88.6	111.4	89.0	111.0	89.4	110.6	89.9	110.1
1.4	87.8	112.2	87.9	112.1	88.1	111.9	88.3	111.7	88.6	111.4	88.9	111.1	89.2	110.8	89.6	110.4	90.0	110.0
1.5	88.0	112.0	88.2	111.8	88.4	111.6	88.6	111.4	88.8	111.2	89.1	110.9	89.4	110.6	89.8	110.2	90.2	109.8
1.6	88.3	111.7	88.5	111.5	88.7	111.3	88.9	111.1	89.1	110.9	89.4	110.6	89.7	110.3	90.0	110.0	90.4	109.6
1.7	88.6	111.4	88.8	111.2	88.9	111.1	89.1	110.9	89.4	110.6	89.6	110.4	89.9	110.1	90.2	109.8	90.6	109.4
1.8	88.9	111.1	89.1	110.9	89.2	110.8	89.4	110.6	89.6	110.4	89.9	110.1	90.2	109.8	90.5	109.5	90.8	109.2
1.9	89.2	110.8	89.4	110.6	89.5	110.5	89.7	110.3	89.9	110.1	90.1	109.9	90.4	109.6	90.7	109.3	91.0	109.0
2.0	89.5	110.5	89.6	110.4	89.8	110.2	90.0	110.0	90.2	109.8	90.4	109.6	90.7	109.3	91.0	109.0	91.3	108.7
2.1	89.8	110.2	89.9	110.1	90.1	109.9	90.3	109.7	90.5	109.5	90.7	109.3	90.9	109.1	91.2	108.8	91.5	108.5
2.2	90.1	109.9	90.2	109.8	90.4	109.6	90.6	109.4	90.7	109.3	91.0	109.0	91.2	108.8	91.5	108.5	91.8	108.2
2.3	90.4	109.6	90.5	109.5	90.7	109.3	90.8	109.2	91.0	109.0	91.2	108.8	91.5	108.5	91.7	108.3	92.0	108.0
2.4	90.7	109.3	90.8	109.2	91.0	109.0	91.1	108.9	91.3	108.7	91.5	108.5	91.7	108.3	92.0	108.0	92.3	107.7
2.5	91.0	109.0	91.1	108.9	91.2	108.8	91.4	108.6	91.6	108.4	91.8	108.2	92.0	108.0	92.2	107.8	92.5	107.5
2.6	91.2	108.8	91.4	108.6	91.5	108.5	91.7	108.3	91.9	108.1	92.1	107.9	92.3	107.7	92.5	107.5	92.8	107.2
2.7	91.5	108.5	91.7	108.3	91.8	108.2	92.0	108.0	92.2	107.8	92.4	107.6	92.6	107.4	92.8	107.2	93.0	107.0
2.8	91.8	108.2	92.0	108.0	92.1	107.9	92.3	107.7	92.4	107.6	92.6	107.4	92.8	107.2	93.1	106.9	93.3	106.7
2.9	92.1	107.9	92.3	107.7	92.4	107.6	92.6	107.4	92.7	107.3	92.9	107.1	93.1	106.9	93.3	106.7	93.6	106.4
3.0	92.4	107.6	92.5	107.5	92.7	107.3	92.9	107.1	93.0	107.0	93.2	106.8	93.4	106.6	93.6	106.4	93.8	106.2
3.1	92.7	107.3	92.8	107.2	93.0	107.0	93.1	106.9	93.3	106.7	93.5	106.5	93.7	106.3	93.9	106.1	94.1	105.9
3.2	93.0	107.0	93.1	106.9	93.3	106.7	93.4	106.6	93.6	106.4	93.8	106.2	94.0	106.0	94.2	105.8	94.4	105.6
3.3	93.3	106.7	93.4	106.6	93.6	106.4	93.7	106.3	93.9	106.1	94.1	105.9	94.2	105.8	94.4	105.6	94.7	105.3
3.4	93.6	106.4	93.7	106.3	93.9	106.1	94.0	106.0	94.2	105.8	94.3	105.7	94.5	105.5	94.7	105.3	94.9	105.1
3.5	93.9	106.1	94.0	106.0	94.1	105.9	94.3	105.7	94.5	105.5	94.6	105.4	94.8	105.2	95.0	105.0	95.2	104.8
3.6	94.2	105.8	94.3	105.7	94.4	105.6	94.6	105.4	94.8	105.2	94.9	105.1	95.1	104.9	95.3	104.7	95.5	104.5
3.7	94.5	105.5	94.6	105.4	94.7	105.3	94.9	105.1	95.0	105.0	95.2	104.8	95.4	104.6	95.6	104.4	95.8	104.2

ACCEPTANCE LIMITS FOR CONTENT UNIFORMITY

SAMPLING PLAN 2

TARGET=100.0, LOWER BOUND = 95.0, CONFIDENCE LEVEL = 95.0

TABLE ENTRIES ARE LOWER(LL) AND UPPER(UL) LIMITS ON THE MEAN

OF 40 ASSAYS- 4 ASSAYS AT EACH OF 10 DIFFERENT LOCATIONS

SE IS THE POOLED WITHIN LOCATION STANDARD DEVIATION

STANDARD DEVIATIONS AND MEANS ARE EXPRESSED IN % CLAIM

STANDARD DEVIATION OF LOCATION MEANS

	0.1		0.2		0.3		0.4		0.5		0.6		0.7		0.8		0.9	
SE	LL	UL	LL	UL	LL	UL	LL	UL	LL	UL	LL	UL	LL	UL	LL	UL	LL	UL
3.8	94.7	105.3	94.9	105.1	95.0	105.0	95.2	104.8	95.3	104.7	95.5	104.5	95.7	104.3	95.9	104.1	96.1	103.9
3.9	95.0	105.0	95.2	104.8	95.3	104.7	95.5	104.5	95.6	104.4	95.8	104.2	96.0	104.0	96.1	103.9	96.3	103.7
4.0	95.3	104.7	95.5	104.5	95.6	104.4	95.8	104.2	95.9	104.1	96.1	103.9	96.3	103.7	96.4	103.6	96.6	103.4
4.1	95.6	104.4	95.8	104.2	95.9	104.1	96.1	103.9	96.2	103.8	96.4	103.6	96.5	103.5	96.7	103.3	96.9	103.1
4.2	95.9	104.1	96.1	103.9	96.2	103.8	96.3	103.7	96.5	103.5	96.7	103.3	96.8	103.2	97.0	103.0	97.2	102.8
4.3	96.2	103.8	96.4	103.6	96.5	103.5	96.6	103.4	96.8	103.2	97.0	103.0	97.1	102.9	97.3	102.7	97.5	102.5
4.4	96.5	103.5	96.6	103.4	96.8	103.2	96.9	103.1	97.1	102.9	97.2	102.8	97.4	102.6	97.6	102.4	97.8	102.2
4.5	96.8	103.2	96.9	103.1	97.1	102.9	97.2	102.8	97.4	102.6	97.5	102.5	97.7	102.3	97.9	102.1	98.1	101.9
4.6	97.1	102.9	97.2	102.8	97.4	102.6	97.5	102.5	97.7	102.3	97.8	102.2	98.0	102.0	98.2	101.8	98.4	101.6
4.7	97.4	102.6	97.5	102.5	97.7	102.3	97.8	102.2	98.0	102.0	98.1	101.9	98.3	101.7	98.5	101.5	98.7	101.3
4.8	97.7	102.3	97.8	102.2	98.0	102.0	98.1	101.9	98.3	101.7	98.4	101.6	98.6	101.4	98.8	101.2	99.0	101.0
4.9	98.0	102.0	98.2	101.8	98.3	101.7	98.4	101.6	98.6	101.4	98.8	101.2	98.9	101.1	99.1	100.9	99.3	100.7
5.0	98.3	101.7	98.5	101.5	98.6	101.4	98.8	101.2	98.9	101.1	99.1	100.9	99.3	100.7	99.4	100.6	99.6	100.4
5.1	98.7	101.3	98.9	101.1	99.0	101.0	99.2	100.8	99.3	100.7	99.5	100.5	99.7	100.3	99.9	100.1		
5.2	99.2	100.8	99.4	100.6	99.5	100.5	99.7	100.3	99.9	100.1								

ACCEPTANCE LIMITS FOR CONTENT UNIFORMITY

SAMPLING PLAN 2

TARGET=100.0, LOWER BOUND = 95.0, CONFIDENCE LEVEL = 95.0

TABLE ENTRIES ARE LOWER(LL) AND UPPER(UL) LIMITS ON THE MEAN

OF 40 ASSAYS- 4 ASSAYS AT EACH OF 10 DIFFERENT LOCATIONS

SE IS THE POOLED WITHIN LOCATION STANDARD DEVIATION

STANDARD DEVIATIONS AND MEANS ARE EXPRESSED IN % CLAIM

STANDARD DEVIATION OF LOCATION MEANS

	1.0		1.1		1.2		1.3		1.4		1.5		1.6		1.7		1.8	
SE	LL	UL	LL	UL	LL	UL	LL	UL	LL	UL	LL	UL	LL	UL	LL	UL	LL	UL
0.1	89.4	110.6	90.0	110.0	90.6	109.4	91.2	108.8	91.8	108.2	92.4	107.6	92.9	107.1	93.5	106.5	94.1	105.9
0.2	89.4	110.6	90.0	110.0	90.6	109.4	91.2	108.8	91.8	108.2	92.4	107.6	93.0	107.0	93.5	106.5	94.1	105.9
0.3	89.5	110.5	90.0	110.0	90.6	109.4	91.2	108.8	91.8	108.2	92.4	107.6	93.0	107.0	93.6	106.4	94.1	105.9
0.4	89.5	110.5	90.1	109.9	90.7	109.3	91.2	108.8	91.8	108.2	92.4	107.6	93.0	107.0	93.6	106.4	94.2	105.8
0.5	89.6	110.4	90.1	109.9	90.7	109.3	91.3	108.7	91.9	108.1	92.4	107.6	93.0	107.0	93.6	106.4	94.2	105.8
0.6	89.6	110.4	90.2	109.8	90.8	109.2	91.3	108.7	91.9	108.1	92.5	107.5	93.1	106.9	93.6	106.4	94.2	105.8
0.7	89.7	110.3	90.2	109.8	90.8	109.2	91.4	108.6	92.0	108.0	92.5	107.5	93.1	106.9	93.7	106.3	94.3	105.7
0.8	89.8	110.2	90.3	109.7	90.9	109.1	91.4	108.6	92.0	108.0	92.6	107.4	93.2	106.8	93.7	106.3	94.3	105.7
0.9	89.9	110.1	90.4	109.6	91.0	109.0	91.5	108.5	92.1	107.9	92.6	107.4	93.2	106.8	93.8	106.2	94.4	105.6
1.0	90.0	110.0	90.5	109.5	91.0	109.0	91.6	108.4	92.1	107.9	92.7	107.3	93.3	106.7	93.8	106.2	94.4	105.6
1.1	90.1	109.9	90.6	109.4	91.1	108.9	91.7	108.3	92.2	107.8	92.8	107.2	93.3	106.7	93.9	106.1	94.5	105.5
1.2	90.2	109.8	90.7	109.3	91.2	108.8	91.8	108.2	92.3	107.7	92.9	107.1	93.4	106.6	94.0	106.0	94.5	105.5
1.3	90.3	109.7	90.8	109.2	91.4	108.6	91.9	108.1	92.4	107.6	93.0	107.0	93.5	106.5	94.1	105.9	94.6	105.4
1.4	90.5	109.5	91.0	109.0	91.5	108.5	92.0	108.0	92.5	107.5	93.1	106.9	93.6	106.4	94.1	105.9	94.7	105.3
1.5	90.7	109.3	91.1	108.9	91.6	108.4	92.1	107.9	92.6	107.4	93.2	106.8	93.7	106.3	94.2	105.8	94.8	105.2
1.6	90.8	109.2	91.3	108.7	91.8	108.2	92.3	107.7	92.8	107.2	93.3	106.7	93.8	106.2	94.3	105.7	94.9	105.1
1.7	91.0	109.0	91.5	108.5	91.9	108.1	92.4	107.6	92.9	107.1	93.4	106.6	93.9	106.1	94.4	105.6	95.0	105.0
1.8	91.2	108.8	91.6	108.4	92.1	107.9	92.5	107.5	93.0	107.0	93.5	106.5	94.0	106.0	94.6	105.4	95.1	104.9
1.9	91.4	108.6	91.8	108.2	92.3	107.7	92.7	107.3	93.2	106.8	93.7	106.3	94.2	105.8	94.7	105.3	95.2	104.8
2.0	91.6	108.4	92.0	108.0	92.4	107.6	92.9	107.1	93.3	106.7	93.8	106.2	94.3	105.7	94.8	105.2	95.3	104.7
2.1	91.9	108.1	92.2	107.8	92.6	107.4	93.1	106.9	93.5	106.5	94.0	106.0	94.4	105.6	94.9	105.1	95.4	104.6
2.2	92.1	107.9	92.4	107.6	92.8	107.2	93.2	106.8	93.7	106.3	94.1	105.9	94.6	105.4	95.1	104.9	95.6	104.4
2.3	92.3	107.7	92.7	107.3	93.0	107.0	93.4	106.6	93.9	106.1	94.3	105.7	94.8	105.2	95.2	104.8	95.7	104.3
2.4	92.6	107.4	92.9	107.1	93.3	106.7	93.6	106.4	94.0	106.0	94.5	105.5	94.9	105.1	95.4	104.6	95.9	104.1
2.5	92.8	107.2	93.1	106.9	93.5	106.5	93.8	106.2	94.2	105.8	94.7	105.3	95.1	104.9	95.6	104.4	96.0	104.0
2.6	93.1	106.9	93.4	106.6	93.7	106.3	94.1	105.9	94.4	105.6	94.9	105.1	95.3	104.7	95.7	104.3	96.2	103.8
2.7	93.3	106.7	93.6	106.4	93.9	106.1	94.3	105.7	94.7	105.3	95.1	104.9	95.5	104.5	95.9	104.1	96.4	103.6
2.8	93.6	106.4	93.9	106.1	94.2	105.8	94.5	105.5	94.9	105.1	95.3	104.7	95.7	104.3	96.1	103.9	96.5	103.5
2.9	93.8	106.2	94.1	105.9	94.4	105.6	94.7	105.3	95.1	104.9	95.5	104.5	95.9	104.1	96.3	103.7	96.7	103.3
3.0	94.1	105.9	94.4	105.6	94.7	105.3	95.0	105.0	95.3	104.7	95.7	104.3	96.1	103.9	96.5	103.5	96.9	103.1
3.1	94.4	105.6	94.6	105.4	94.9	105.1	95.2	104.8	95.5	104.5	95.9	104.1	96.3	103.7	96.7	103.3	97.1	102.9
3.2	94.6	105.4	94.9	105.1	95.2	104.8	95.5	104.5	95.8	104.2	96.1	103.9	96.5	103.5	96.9	103.1	97.3	102.7
3.3	94.9	105.1	95.1	104.9	95.4	104.6	95.7	104.3	96.0	104.0	96.4	103.6	96.7	103.3	97.1	102.9	97.5	102.5
3.4	95.2	104.8	95.4	104.6	95.7	104.3	96.0	104.0	96.3	103.7	96.6	103.4	96.9	103.1	97.3	102.7	97.7	102.3
3.5	95.4	104.6	95.7	104.3	95.9	104.1	96.2	103.8	96.5	103.5	96.8	103.2	97.2	102.8	97.5	102.5	97.9	102.1
3.6	95.7	104.3	96.0	104.0	96.2	103.8	96.5	103.5	96.8	103.2	97.1	102.9	97.4	102.6	97.8	102.2	98.1	101.9
3.7	96.0	104.0	96.2	103.8	96.5	103.5	96.7	103.3	97.0	103.0	97.3	102.7	97.6	102.4	98.0	102.0	98.3	101.7

[illegible]

SAMPLING PLAN 2

STANDARD DEVIATION OF LOCATION MEANS

	1.9		2.0		2.1		2.2		2.3		2.4		2.5		2.6		2.7	
SE	LL	UL	LL	UL	LL	UL	LL	UL	LL	UL	LL	UL	LL	UL	LL	UL	LL	UL
0.1	94.7	105.3	95.3	104.7	95.9	104.1	96.5	103.5	97.1	102.9	97.7	102.3	98.2	101.8	98.8	101.2	99.4	100.6
0.2	94.7	105.3	95.3	104.7	95.9	104.1	96.5	103.5	97.1	102.9	97.7	102.3	98.2	101.8	98.8	101.2	99.4	100.6
0.3	94.7	105.3	95.3	104.7	95.9	104.1	96.5	103.5	97.1	102.9	97.7	102.3	98.3	101.7	98.9	101.1	99.4	100.6
0.4	94.7	105.3	95.3	104.7	95.9	104.1	96.5	103.5	97.1	102.9	97.7	102.3	98.3	101.7	98.9	101.1	99.5	100.5
0.5	94.8	105.2	95.4	104.6	95.9	104.1	96.5	103.5	97.1	102.9	97.7	102.3	98.3	101.7	98.9	101.1	99.5	100.5
0.6	94.8	105.2	95.4	104.6	96.0	104.0	96.6	103.4	97.1	102.9	97.7	102.3	98.3	101.7	98.9	101.1	99.5	100.5
0.7	94.8	105.2	95.4	104.6	96.0	104.0	96.6	103.4	97.2	102.8	97.8	102.2	98.3	101.7	98.9	101.1	99.5	100.5
0.8	94.9	105.1	95.5	104.5	96.0	104.0	96.6	103.4	97.2	102.8	97.8	102.2	98.4	101.6	99.0	101.0	99.6	100.4
0.9	94.9	105.1	95.5	104.5	96.1	103.9	96.7	103.3	97.2	102.8	97.8	102.2	98.4	101.6	99.0	101.0	99.6	100.4
1.0	95.0	105.0	95.6	104.4	96.1	103.9	96.7	103.3	97.3	102.7	97.9	102.1	98.5	101.5	99.0	101.0	99.6	100.4
1.1	95.0	105.0	95.6	104.4	96.2	103.8	96.8	103.2	97.3	102.7	97.9	102.1	98.5	101.5	99.1	100.9	99.7	100.3
1.2	95.1	104.9	95.7	104.3	96.2	103.8	96.8	103.2	97.4	102.6	98.0	102.0	98.5	101.5	99.1	100.9	99.7	100.3
1.3	95.2	104.8	95.7	104.3	96.3	103.7	96.9	103.1	97.4	102.6	98.0	102.0	98.6	101.4	99.2	100.8	99.8	100.2
1.4	95.3	104.7	95.8	104.2	96.4	103.6	96.9	103.1	97.5	102.5	98.1	101.9	98.7	101.3	99.2	100.8	99.8	100.2
1.5	95.3	104.7	95.9	104.1	96.4	103.6	97.0	103.0	97.6	102.4	98.1	101.9	98.7	101.3	99.3	100.7	99.9	100.1
1.6	95.4	104.6	96.0	104.0	96.5	103.5	97.1	102.9	97.7	102.3	98.2	101.8	98.8	101.2	99.4	100.6	99.9	100.1
1.7	95.5	104.5	96.1	103.9	96.6	103.4	97.2	102.8	97.7	102.3	98.3	101.7	98.9	101.1	99.4	100.6	100.0	100.0
1.8	95.6	104.4	96.2	103.8	96.7	103.3	97.3	102.7	97.8	102.2	98.4	101.6	98.9	101.1	99.5	100.5		
1.9	95.7	104.3	96.3	103.7	96.8	103.2	97.3	102.7	97.9	102.1	98.5	101.5	99.0	101.0	99.6	100.4		
2.0	95.8	104.2	96.4	103.6	96.9	103.1	97.4	102.6	98.0	102.0	98.5	101.5	99.1	100.9	99.7	100.3		
2.1	96.0	104.0	96.5	103.5	97.0	103.0	97.5	102.5	98.1	101.9	98.6	101.4	99.2	100.8	99.7	100.3		
2.2	96.1	103.9	96.6	103.4	97.1	102.9	97.7	102.3	98.2	101.8	98.7	101.3	99.3	100.7	99.8	100.2		
2.3	96.2	103.8	96.7	103.3	97.2	102.8	97.8	102.2	98.3	101.7	98.8	101.2	99.4	100.6	99.9	100.1		
2.4	96.4	103.6	96.9	103.1	97.4	102.6	97.9	102.1	98.4	101.6	99.0	101.0	99.5	100.5	100.0	100.0		
2.5	96.5	103.5	97.0	103.0	97.5	102.5	98.0	102.0	98.5	101.5	99.1	100.9	99.6	100.4				
2.6	96.7	103.3	97.1	102.9	97.6	102.4	98.1	101.9	98.7	101.3	99.2	100.8	99.7	100.3				
2.7	96.8	103.2	97.3	102.7	97.8	102.2	98.3	101.7	98.8	101.2	99.3	100.7	99.8	100.2				
2.8	97.0	103.0	97.5	102.5	97.9	102.1	98.4	101.6	98.9	101.1	99.4	100.6	100.0	100.0				
2.9	97.2	102.8	97.6	102.4	98.1	101.9	98.6	101.4	99.1	100.9	99.6	100.4						
3.0	97.3	102.7	97.8	102.2	98.3	101.7	98.7	101.3	99.2	100.8	99.7	100.3						
3.1	97.5	102.5	98.0	102.0	98.4	101.6	98.9	101.1	99.4	100.6	99.9	100.1						
3.2	97.7	102.3	98.1	101.9	98.6	101.4	99.1	100.9	99.5	100.5	100.0	100.0						
3.3	97.9	102.1	98.3	101.7	98.8	101.2	99.2	100.8	99.7	100.3								
3.4	98.1	101.9	98.5	101.5	98.9	101.1	99.4	100.6	99.9	100.1								
3.5	98.3	101.7	98.7	101.3	99.1	100.9	99.6	100.4	100.0	100.0								
3.6	98.5	101.5	98.9	101.1	99.3	100.7	99.8	100.2										
3.7	98.7	101.3	99.1	100.9	99.5	100.5	100.0	100.0										

4.2 99.9 100.1

0.4 100.0 100.0

ACCEPTANCE LIMITS FOR CONTENT UNIFORMITY
 SAMPLING PLAN 2
 PROBABILITY OF PASSING ACCEPTANCE LIMIT TABLE
 WITH 4 ASSAYS AT EACH OF 10 LOCATIONS
 CONFIDENCE LEVEL = 95.0 & LOWER BOUND = 95.0

Obs	MEAN	WITHIN LOCATION STD DEV	BETWEEN LOCATION STD DEV	PROBABILITY OF PASSING
1	95	2.2	2.2	0.09180
2	100	2.2	2.2	0.55987

ACCEPTANCE LIMITS FOR CONTENT UNIFORMITY
 SAMPLING PLAN 2 (10 LOCATIONS, 4 PER LOCATION)
 PROPORTION OF FUTURE SAMPLES PASSING THE USP TEST
 WITH 95.0% ASSURANCE
 FOR GIVEN SAMPLE MEAN, WITHIN AND BETWEEN LOCATION STD DEV

SAMPLE MEAN	SAMPLE WITHIN LOCATION STD DEV	SAMPLE BETWEEN LOCATION STD DEV	LOWER BOUND
100	2.2	2.46	0.98750

Dissolution/Sampling Plan 1

If **Dissolution/Sampling Plan 1** is selected, the following screen appears:

The screenshot shows the SAS interface with the 'DISSOLUTION ACCEPTANCE LIMIT PROGRAM FOR SAMPLING PLAN 1 (ONE PER LOCATION)' dialog box. The dialog box has a title bar with 'SAS' and standard window controls. Below the title bar is a menu bar with 'File', 'View', 'Tools', 'Solutions', 'Window', and 'Help'. A toolbar with various icons is located below the menu bar. The main area of the dialog box contains the following text and input fields:

Command ==>

DISSOLUTION ACCEPTANCE LIMIT PROGRAM FOR
SAMPLING PLAN 1 (ONE PER LOCATION)

ENTER Q VALUE:

ENTER SAMPLE SIZE:

ENTER BOUND ON FUTURE PERCENTAGE PASSING (50.0-99.0):

ENTER CONFIDENCE LEVEL (50.0-99.0):

DO YOU WANT TO PRINT THE ACCEPTANCE LIMIT TABLE? ☒ Y ☐ N

DO YOU WANT TO EVALUATE THE ACCEPTANCE LIMIT TABLE? ☐ Y ☒ N

DO YOU WANT THE LOWER BOUND FOR A SPECIFIC SAMPLE RESULT? ☐ Y ☒ N

At the bottom of the dialog box are two buttons: 'Run' and 'Cancel'.

The bottom of the SAS window shows a taskbar with several open windows: 'Output - (Untitled)', 'Log - (Untitled)', 'CuDAL.sas', and 'Program Editor - (Untitled)'. The status bar at the bottom indicates the current directory is 'C:\Program Files\SAS Institute\SAS\V8' and the time is 3:49 PM.

The user enters the value of Q, sample size (i.e., number of dosage units tested), the coverage percentage (usually 90 or 95), and the confidence level (usually 90 or 95). There are three choices for SAS output 1) The acceptance limit table, 2) an evaluation of the acceptance limit table, and 3) a calculation of the lower bound based on sample results. The user can pick more than one of these options. The second option calculates the probability of passing the acceptance limit table based on the sample size, coverage, and confidence level selected. The following table appears if this option is selected.

TO EVALUATE LIMITS, THE USER MUST SPECIFY THE RANGE OF POSSIBLE POPULATION VALUES FOR THE MEAN AND CV

ENTER ALL VALUES AS POSITIVE INTEGERS

ENTER LOWER BOUND FOR MEAN: 950

ENTER UPPER BOUND FOR MEAN: 1000

ENTER INCREMENT FOR MEAN: 50

ENTER DIVISOR FOR MEAN: 10

ENTER LOWER BOUND FOR CV: 10

ENTER UPPER BOUND FOR CV: 40

ENTER INCREMENT FOR CV: 30

ENTER DIVISOR FOR CV: 10

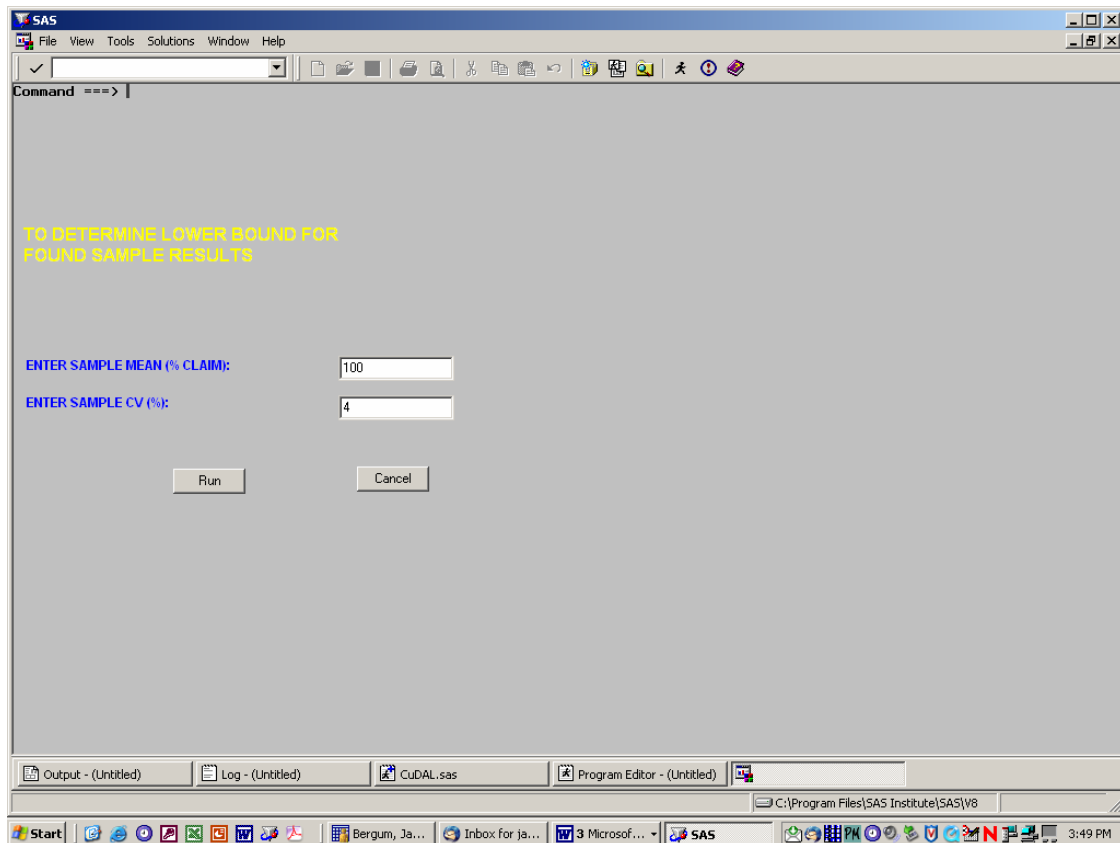
Run Cancel

Output - (Untitled) Log - (Untitled) CuDAL.sas Program Editor - (Untitled)

C:\Program Files\SAS Institute\SAS\VB 3:49 PM

The user provides “true” values for the population mean and coefficient of variation (CV) - also called relative standard deviation (RSD) and then using these “true” values, the program calculates the probability that the sample results will fall within the acceptance limits. The entries on this window must all be integers. The lower bound, upper bound, increment, and divisor are entered for both the desired population means and CV’s. The default values indicate that an evaluation is performed using population means of 95.0 and 100.0 and CV’s of 1.0 and 4.0 since the mean goes from 950 to 1000 by 50 and dividing by 10 (i.e., $950/10$, then $1000/10$) and the CV goes from 10 to 40 by 30 (i.e., $10/10$, then $40/10$).

If the 3rd option - **Lower Bound for Sample Result** - is selected, then the following screen appears:



The user enters the sample mean and sample CV.

Sample output from each of these three options are given on the following pages.

ACCEPTANCE LIMITS FOR DISSOLUTION (N = 6, Q = 80.0)
 SAMPLING PLAN 1
 (MEETING LIMITS GUARANTEES WITH 95.0 % ASSURANCE,
 THAT AT LEAST 95.0% OF ALL FUTURE SAMPLES TESTED
 FOR DISSOLUTION WILL PASS THE USP TEST)
 TABLE ENTRY IS UPPER LIMIT ON CV OF 6 DISSOLUTION ASSAYS

MEAN (% CLAIM)	CV (%)	MEAN (% CLAIM)	CV (%)	MEAN (% CLAIM)	CV (%)	MEAN (% CLAIM)	CV (%)	MEAN (% CLAIM)	CV (%)
80.2	0.09	84.2	1.80	88.2	3.34	92.2	4.28	96.2	4.69
80.4	0.18	84.4	1.88	88.4	3.41	92.4	4.31	96.4	4.70
80.6	0.27	84.6	1.96	88.6	3.47	92.6	4.33	96.6	4.72
80.8	0.36	84.8	2.04	88.8	3.54	92.8	4.36	96.8	4.73
81.0	0.44	85.0	2.12	89.0	3.60	93.0	4.38	97.0	4.75
81.2	0.53	85.2	2.20	89.2	3.66	93.2	4.41	97.2	4.77
81.4	0.62	85.4	2.28	89.4	3.71	93.4	4.43	97.4	4.78
81.6	0.71	85.6	2.36	89.6	3.77	93.6	4.45	97.6	4.80
81.8	0.79	85.8	2.44	89.8	3.82	93.8	4.47	97.8	4.81
82.0	0.88	86.0	2.52	90.0	3.87	94.0	4.49	98.0	4.82
82.2	0.96	86.2	2.59	90.2	3.92	94.2	4.51	98.2	4.84
82.4	1.05	86.4	2.67	90.4	3.96	94.4	4.53	98.4	4.85
82.6	1.13	86.6	2.75	90.6	4.00	94.6	4.55	98.6	4.87
82.8	1.22	86.8	2.82	90.8	4.04	94.8	4.57	98.8	4.88
83.0	1.30	87.0	2.90	91.0	4.08	95.0	4.59	99.0	4.90
83.2	1.39	87.2	2.98	91.2	4.12	95.2	4.60	99.2	4.91
83.4	1.47	87.4	3.05	91.4	4.15	95.4	4.62	99.4	4.92
83.6	1.55	87.6	3.12	91.6	4.19	95.6	4.64	99.6	4.94
83.8	1.63	87.8	3.20	91.8	4.22	95.8	4.65	99.8	4.95
84.0	1.72	88.0	3.27	92.0	4.25	96.0	4.67	100.0	4.97

ACCEPTANCE LIMITS FOR DISSOLUTION (N = 6, Q = 80.0)

SAMPLING PLAN 1

PROBABILITY OF PASSING ACCEPTANCE LIMIT TABLE

CONFIDENCE LEVEL = 95.0 AND LOWER BOUND = 95.0

U	CV	PROBABILITY
		OF PASSING
95	1	1.00000
100	1	1.00000
95	4	0.73988
100	4	0.81098

ACCEPTANCE LIMITS FOR DISSOLUTION (N = 6, Q = 80.0)

SAMPLING PLAN 1

PROPORTION OF FUTURE SAMPLES PASSING THE USP TEST
FOR A GIVEN SAMPLE MEAN AND CV WITH 95.0% ASSURANCE

SAMPLE MEAN (% CLAIM)	SAMPLE STD DEV (% CLAIM)	CV	LOWER BOUND
100	4	4	0.99824

Dissolution/Sampling Plan 2

If **Dissolution/Sampling Plan 2** is selected, the following screen appears:

The screenshot shows the SAS DISSOLUTION ACCEPTANCE LIMIT PROGRAM FOR SAMPLING PLAN 2 dialog box. The title bar reads "SAS". The menu bar includes File, View, Tools, Solutions, Window, and Help. The toolbar contains various icons for file operations and execution. The main area has a yellow title "DISSOLUTION ACCEPTANCE LIMIT PROGRAM FOR SAMPLING PLAN 2 [GREATER THAN ONE SAMPLE PER LOCATION]". Below this, there are input fields for "ENTER Q:", "ENTER NUMBER OF LOCATIONS:", "ENTER NUMBER PER LOCATION:", "ENTER BOUND ON FUTURE PERCENTAGE PASSING (50.0-99.0):", "ENTER CONFIDENCE LEVEL (50.0-99.0):", "ENTER INCREMENT FOR SE:", and "ENTER INCREMENT FOR BETWEEN LOCATION STD DEV:". Each field has a corresponding text input box with values 80, 10, 6, 95, 95, 0.25, and 0.25 respectively. There are three radio button options: "DO YOU WANT TO PRINT THE ACCEPTANCE LIMIT TABLE?" (Y selected), "DO YOU WANT TO EVALUATE THE ACCEPTANCE LIMIT TABLE?" (N selected), and "DO YOU WANT THE LOWER BOUND FOR A SPECIFIC SAMPLE RESULT?" (N selected). At the bottom are "Run" and "Cancel" buttons. The status bar at the bottom shows the file path "C:\Program Files\SAS Institute\SAS\VB8" and the time "3:50 PM".

Command ===>

DISSOLUTION ACCEPTANCE LIMIT PROGRAM FOR SAMPLING PLAN 2 [GREATER THAN ONE SAMPLE PER LOCATION]

ENTER Q: 80

ENTER NUMBER OF LOCATIONS: 10

ENTER NUMBER PER LOCATION: 6

ENTER BOUND ON FUTURE PERCENTAGE PASSING (50.0-99.0): 95

ENTER CONFIDENCE LEVEL (50.0-99.0): 95

ENTER INCREMENT FOR SE: 0.25

ENTER INCREMENT FOR BETWEEN LOCATION STD DEV: 0.25

DO YOU WANT TO PRINT THE ACCEPTANCE LIMIT TABLE? ☒ Y ☐ N

DO YOU WANT TO EVALUATE THE ACCEPTANCE LIMIT TABLE? ☐ Y ☒ N

DO YOU WANT THE LOWER BOUND FOR A SPECIFIC SAMPLE RESULT? ☐ Y ☒ N

Run Cancel

Output - (Untitled) Log - (Untitled) CuDAL.sas Program Editor - (Untitled)

C:\Program Files\SAS Institute\SAS\VB8

Start [Taskbar icons] 3:50 PM

The user enters Q, the number of locations, the number of dosage units per location, the coverage probability, and the confidence level. There are three choices for SAS output 1) The acceptance limit table, 2) an evaluation of the acceptance limit table, and 3) a calculation of the lower bound based on sample results. The user can pick more than one of these options. The second option calculates the probability of passing the acceptance limit table based on the sample size, coverage, and confidence level selected. The following table appears if this option is selected.

Command ==>

TO EVALUATE LIMITS, THE USER MUST SPECIFY THE RANGE OF POSSIBLE POPULATION VALUES FOR THE MEAN, WITHIN LOCATION STD DEV AND BETWEEN LOCATION STD DEV

ENTER ALL VALUES AS POSITIVE INTEGERS

ENTER LOWER BOUND FOR MEAN: 950

ENTER UPPER BOUND FOR MEAN: 1000

ENTER INCREMENT FOR MEAN: 50

ENTER DIVISOR FOR MEAN: 10

ENTER LOWER BOUND FOR WITHIN STD DEV: 22

ENTER UPPER BOUND FOR WITHIN STD DEV: 22

ENTER INCREMENT FOR WITHIN STD DEV: 10

ENTER DIVISOR FOR WITHIN STD DEV: 10

ENTER LOWER BOUND FOR BETWEEN STD DEV: 22

ENTER UPPER BOUND FOR BETWEEN STD DEV: 22

ENTER INCREMENT FOR BETWEEN STD DEV: 10

ENTER DIVISOR FOR BETWEEN STD DEV: 10

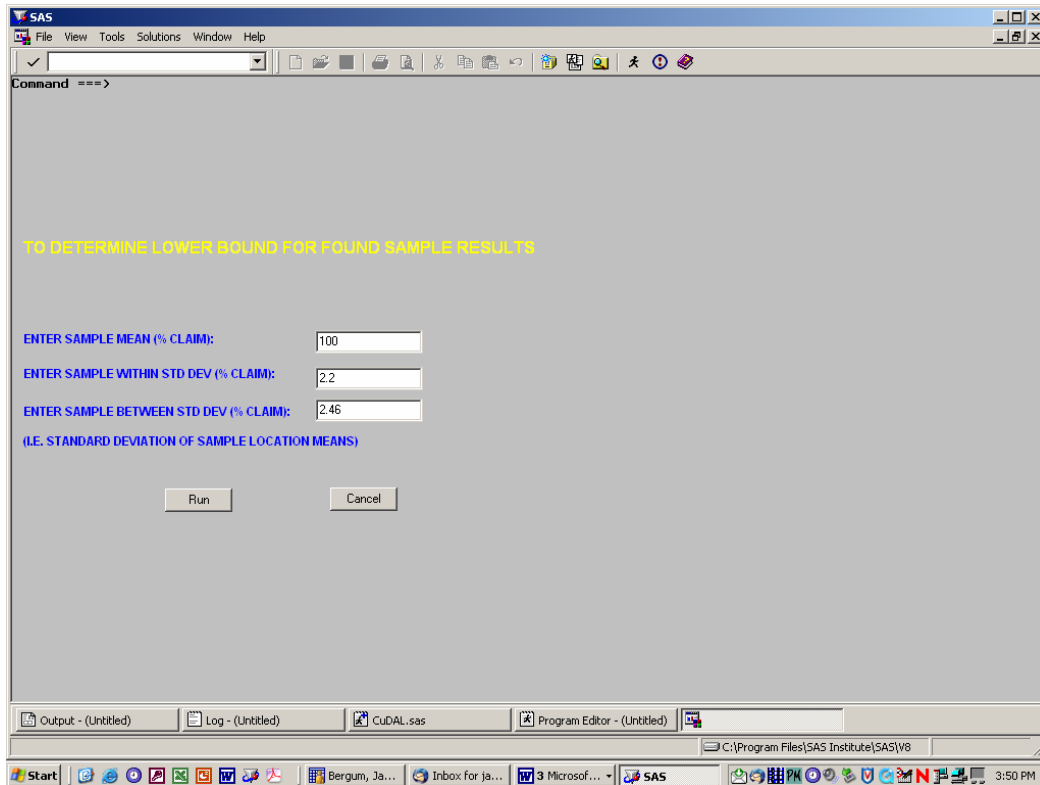
Run Cancel

Output - (Untitled) Log - (Untitled) CuDAL.sas Program Editor - (Untitled) C:\Program Files\SAS Institute\SAS\VB8

Start [Icons] Bergum, Ja... Inbox for ja... 3 Microsoft... SAS [Icons] 3:50 PM

The user provides “true” values for the population mean, coefficient of variation (CV) within locations, and CV for the between location. Using these “true” values, the program calculates the probability that the sample results will fall within the acceptance limits. The entries on this window must all be integers. The lower bound, upper bound, increment, and divisor are entered for both the desired population means and within/between location CV’s. The default values indicate that an evaluation is performed using population means of 95.0 and 100.0, within location CV of 2.2, and between location CV’ of 2.2 since the mean goes from 950 to 1000 by 50 and dividing by 10 (i.e., $950/10$, then $1000/10$) and the CV’s go from 22 to 22 by 10 (i.e., only one value - $22/10$).

If the 3rd option - **Lower Bound for Sample Result** - is selected, then the following screen appears:



The user enters the sample mean, within sample standard deviation, and between sample standard deviation [Note: This is just the sample standard deviation of the sample means, not a variance component!!]

Sample output from each of these three options are given on the following pages.

ACCEPTANCE LIMITS FOR DISSOLUTION (Q = 80.0)
SAMPLING PLAN 2
LOWER BOUND = 95.0, CONFIDENCE LEVEL = 95.0
TABLE ENTRIES ARE LOWER LIMITS ON THE MEAN
OF 60 ASSAYS- 6 ASSAYS AT EACH OF 10 DIFFERENT LOCATIONS
SE IS THE POOLED WITHIN LOCATION STANDARD DEVIATION
STANDARD DEVIATIONS AND MEANS ARE EXPRESSED IN % CLAIM

STANDARD DEVIATION OF LOCATION MEANS																	
SE	0.25	0.50	0.75	1.00	1.25	1.50	1.75	2.00	2.25	2.50	2.75	3.00	3.25	3.50	3.75	4.00	4.25
0.25	80.50	80.90	81.40	81.80	82.20	82.70	83.10	83.50	84.00	84.40	84.80	85.30	85.70	86.10	86.60	87.00	87.50
0.50	80.60	81.00	81.40	81.80	82.20	82.70	83.10	83.50	84.00	84.40	84.80	85.30	85.70	86.10	86.60	87.10	87.50
0.75	80.60	81.00	81.40	81.80	82.30	82.70	83.10	83.50	84.00	84.40	84.80	85.30	85.70	86.20	86.60	87.10	87.60
1.00	80.70	81.10	81.50	81.90	82.30	82.70	83.10	83.60	84.00	84.40	84.90	85.30	85.70	86.20	86.60	87.10	87.60
1.25	80.80	81.10	81.50	81.90	82.30	82.70	83.20	83.60	84.00	84.40	84.90	85.30	85.70	86.20	86.60	87.10	87.60
1.50	80.90	81.20	81.60	82.00	82.40	82.80	83.20	83.60	84.00	84.50	84.90	85.30	85.80	86.20	86.60	87.10	87.60
1.75	81.00	81.30	81.60	82.00	82.40	82.80	83.20	83.60	84.10	84.50	84.90	85.30	85.80	86.20	86.70	87.10	87.60
2.00	81.10	81.40	81.70	82.10	82.50	82.90	83.30	83.70	84.10	84.50	84.90	85.40	85.80	86.20	86.70	87.10	87.70
2.25	81.20	81.50	81.80	82.20	82.50	82.90	83.30	83.70	84.10	84.50	85.00	85.40	85.80	86.30	86.70	87.20	87.70
2.50	81.30	81.60	81.90	82.20	82.60	83.00	83.40	83.80	84.20	84.60	85.00	85.40	85.80	86.30	86.70	87.20	87.70
2.75	81.40	81.70	82.00	82.30	82.70	83.00	83.40	83.80	84.20	84.60	85.00	85.50	85.90	86.30	86.80	87.20	87.80
3.00	81.50	81.80	82.10	82.40	82.70	83.10	83.50	83.90	84.30	84.70	85.10	85.50	85.90	86.30	86.80	87.30	87.80
3.25	81.60	81.90	82.20	82.50	82.80	83.20	83.50	83.90	84.30	84.70	85.10	85.50	86.00	86.40	86.80	87.30	87.90
3.50	81.70	82.00	82.30	82.60	82.90	83.20	83.60	84.00	84.40	84.80	85.20	85.60	86.00	86.40	86.90	87.40	87.90

3.75	81.80	82.10	82.30	82.70	83.00	83.30	83.70	84.00	84.40	84.80	85.20	85.60	86.00	86.50	86.90	87.50	88.00
4.00	81.90	82.10	82.40	82.70	83.10	83.40	83.80	84.10	84.50	84.90	85.30	85.70	86.10	86.50	87.00	87.50	88.10
4.25	82.00	82.20	82.50	82.80	83.20	83.50	83.80	84.20	84.60	84.90	85.30	85.70	86.20	86.60	87.10	87.60	88.20

(Continued)

ACCEPTANCE LIMITS FOR DISSOLUTION (Q = 80.0)
SAMPLING PLAN 2
LOWER BOUND = 95.0, CONFIDENCE LEVEL = 95.0
TABLE ENTRIES ARE LOWER LIMITS ON THE MEAN
OF 60 ASSAYS- 6 ASSAYS AT EACH OF 10 DIFFERENT LOCATIONS
SE IS THE POOLED WITHIN LOCATION STANDARD DEVIATION
STANDARD DEVIATIONS AND MEANS ARE EXPRESSED IN % CLAIM

STANDARD DEVIATION OF LOCATION MEANS

	0.25	0.50	0.75	1.00	1.25	1.50	1.75	2.00	2.25	2.50	2.75	3.00	3.25	3.50	3.75	4.00	4.25
SE																	
4.50	82.00	82.30	82.60	82.90	83.20	83.60	83.90	84.30	84.60	85.00	85.40	85.80	86.20	86.70	87.20	87.70	88.30
4.75	82.10	82.40	82.70	83.00	83.30	83.70	84.00	84.30	84.70	85.10	85.50	85.90	86.30	86.70	87.20	87.80	88.40
5.00	82.20	82.50	82.80	83.10	83.40	83.70	84.10	84.40	84.80	85.10	85.50	85.90	86.40	86.80	87.30	87.90	88.60
5.25	82.30	82.60	82.90	83.20	83.50	83.80	84.20	84.50	84.90	85.20	85.60	86.00	86.40	86.90	87.40	88.00	88.70
5.50	82.40	82.70	83.00	83.30	83.60	83.90	84.20	84.60	84.90	85.30	85.70	86.10	86.60	87.00	87.60	88.20	88.90
5.75	82.50	82.80	83.10	83.40	83.70	84.00	84.30	84.70	85.00	85.40	85.80	86.20	86.70	87.20	87.70	88.40	89.10
6.00	82.60	82.90	83.20	83.50	83.80	84.10	84.40	84.80	85.10	85.50	85.90	86.30	86.80	87.30	87.90	88.60	89.30
6.25	82.70	83.00	83.30	83.60	83.90	84.20	84.60	84.90	85.30	85.60	86.00	86.50	87.00	87.50	88.10	88.80	89.60
6.50	82.90	83.10	83.40	83.70	84.00	84.40	84.70	85.00	85.40	85.80	86.20	86.60	87.10	87.70	88.30	89.00	89.90
6.75	83.00	83.30	83.60	83.90	84.20	84.50	84.80	85.20	85.50	85.90	86.40	86.80	87.30	87.90	88.60	89.30	90.20
7.00	83.10	83.40	83.70	84.00	84.30	84.70	85.00	85.30	85.70	86.10	86.60	87.00	87.60	88.20	88.90	89.70	90.60
7.25	83.30	83.60	83.90	84.20	84.50	84.80	85.20	85.50	85.90	86.30	86.80	87.30	87.90	88.50	89.20	90.00	91.00
7.50	83.50	83.80	84.10	84.40	84.70	85.10	85.40	85.80	86.20	86.60	87.10	87.60	88.20	88.80	89.60	90.40	91.40
7.75	83.80	84.10	84.40	84.70	85.00	85.30	85.70	86.10	86.50	86.90	87.40	87.90	88.60	89.30	90.00	90.90	91.80

8.00	84.10	84.40	84.70	85.00	85.30	85.60	86.00	86.40	86.80	87.30	87.80	88.40	89.00	89.70	90.50	91.40	92.30
8.25	84.40	84.70	85.00	85.30	85.70	86.00	86.40	86.80	87.20	87.70	88.20	88.80	89.50	90.20	91.00	91.90	92.80
8.50	84.80	85.10	85.40	85.80	86.10	86.40	86.80	87.20	87.70	88.20	88.70	89.30	90.00	90.70	91.50	92.40	93.40

(Continued)

ACCEPTANCE LIMITS FOR DISSOLUTION (Q = 80.0)
SAMPLING PLAN 2
LOWER BOUND = 95.0, CONFIDENCE LEVEL = 95.0
TABLE ENTRIES ARE LOWER LIMITS ON THE MEAN
OF 60 ASSAYS- 6 ASSAYS AT EACH OF 10 DIFFERENT LOCATIONS
SE IS THE POOLED WITHIN LOCATION STANDARD DEVIATION
STANDARD DEVIATIONS AND MEANS ARE EXPRESSED IN % CLAIM

STANDARD DEVIATION OF LOCATION MEANS																	
	0.25	0.50	0.75	1.00	1.25	1.50	1.75	2.00	2.25	2.50	2.75	3.00	3.25	3.50	3.75	4.00	4.25
SE																	
8.75	85.30	85.60	85.90	86.20	86.60	86.90	87.30	87.80	88.20	88.70	89.30	89.90	90.60	91.30	92.10	93.00	93.90
9.00	85.80	86.10	86.50	86.80	87.10	87.50	87.90	88.30	88.80	89.30	89.90	90.50	91.20	91.90	92.70	93.50	94.50
9.25	86.50	86.80	87.10	87.40	87.80	88.10	88.50	89.00	89.40	90.00	90.50	91.10	91.80	92.50	93.30	94.10	95.00
9.50	87.10	87.40	87.70	88.10	88.40	88.80	89.20	89.60	90.10	90.60	91.20	91.80	92.40	93.20	93.90	94.70	95.60
9.75	87.80	88.10	88.40	88.80	89.10	89.50	89.90	90.30	90.80	91.30	91.90	92.50	93.10	93.80	94.60	95.40	96.20
10.00	88.50	88.80	89.20	89.50	89.80	90.20	90.60	91.10	91.50	92.00	92.60	93.10	93.80	94.50	95.20	96.00	96.80
10.25	89.30	89.60	89.90	90.20	90.60	91.00	91.40	91.80	92.20	92.70	93.30	93.80	94.50	95.10	95.90	96.60	97.40
10.50	90.00	90.30	90.60	91.00	91.30	91.70	92.10	92.50	93.00	93.50	94.00	94.50	95.20	95.80	96.50	97.30	98.10
10.75	90.80	91.10	91.40	91.70	92.10	92.40	92.80	93.30	93.70	94.20	94.70	95.30	95.90	96.50	97.20	97.90	98.70
11.00	91.50	91.80	92.10	92.50	92.80	93.20	93.60	94.00	94.40	94.90	95.40	96.00	96.60	97.20	97.90	98.60	99.40
11.25	92.30	92.60	92.90	93.20	93.60	94.00	94.30	94.80	95.20	95.70	96.20	96.70	97.30	97.90	98.60	99.30	100.00
11.50	93.10	93.40	93.70	94.00	94.30	94.70	95.10	95.50	95.90	96.40	96.90	97.40	98.00	98.60	99.30	100.00	
11.75	93.80	94.10	94.40	94.80	95.10	95.50	95.90	96.30	96.70	97.20	97.60	98.20	98.70	99.30	100.00		
12.00	94.60	94.90	95.20	95.50	95.90	96.30	96.60	97.00	97.50	97.90	98.40	98.90	99.50				

12.25	95.40	95.70	96.00	96.30	96.70	97.00	97.40	97.80	98.20	98.70	99.20	99.70
12.50	96.20	96.50	96.80	97.10	97.40	97.80	98.20	98.60	99.00	99.40	99.90	
12.75	96.90	97.20	97.60	97.90	98.20	98.60	99.00	99.40	99.80			

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(Continued)

ACCEPTANCE LIMITS FOR DISSOLUTION (Q = 80.0)
 SAMPLING PLAN 2
 LOWER BOUND = 95.0, CONFIDENCE LEVEL = 95.0
 TABLE ENTRIES ARE LOWER LIMITS ON THE MEAN
 OF 60 ASSAYS- 6 ASSAYS AT EACH OF 10 DIFFERENT LOCATIONS
 SE IS THE POOLED WITHIN LOCATION STANDARD DEVIATION
 STANDARD DEVIATIONS AND MEANS ARE EXPRESSED IN % CLAIM

STANDARD DEVIATION OF LOCATION MEANS																	
	0.25	0.50	0.75	1.00	1.25	1.50	1.75	2.00	2.25	2.50	2.75	3.00	3.25	3.50	3.75	4.00	4.25
SE																	
13.00	97.70	98.00	98.30	98.70	99.00	99.40	99.70										
13.25	98.50	98.80	99.10	99.50	99.80												
13.50	99.30	99.60	99.90														

(Continued)

ACCEPTANCE LIMITS FOR DISSOLUTION (Q = 80.0)
SAMPLING PLAN 2
LOWER BOUND = 95.0, CONFIDENCE LEVEL = 95.0
TABLE ENTRIES ARE LOWER LIMITS ON THE MEAN
OF 60 ASSAYS- 6 ASSAYS AT EACH OF 10 DIFFERENT LOCATIONS
SE IS THE POOLED WITHIN LOCATION STANDARD DEVIATION
STANDARD DEVIATIONS AND MEANS ARE EXPRESSED IN % CLAIM

	STANDARD DEVIATION OF LOCATION MEANS											
	4.50	4.75	5.00	5.25	5.50	5.75	6.00	6.25	6.50	6.75	7.00	7.25
SE												
0.25	88.10	88.70	89.50	90.30	91.40	92.60	94.00	95.40	96.90	98.40	99.90	
0.50	88.10	88.70	89.50	90.40	91.40	92.60	94.00	95.40	96.90	98.40	99.90	
0.75	88.10	88.70	89.50	90.40	91.40	92.70	94.00	95.50	96.90	98.40	99.90	
1.00	88.10	88.80	89.50	90.40	91.50	92.70	94.10	95.50	97.00	98.50	100.00	
1.25	88.10	88.80	89.50	90.40	91.50	92.80	94.10	95.60	97.00	98.50	100.00	
1.50	88.20	88.80	89.60	90.50	91.60	92.80	94.20	95.60	97.10	98.60		
1.75	88.20	88.90	89.60	90.50	91.60	92.90	94.30	95.70	97.20	98.60		
2.00	88.20	88.90	89.70	90.60	91.70	93.00	94.40	95.80	97.20	98.70		
2.25	88.30	88.90	89.70	90.70	91.80	93.10	94.50	95.90	97.30	98.80		
2.50	88.30	89.00	89.80	90.80	91.90	93.20	94.60	96.00	97.50	98.90		
2.75	88.40	89.10	89.90	90.90	92.00	93.30	94.70	96.10	97.60	99.10		
3.00	88.40	89.10	90.00	91.00	92.20	93.50	94.80	96.30	97.70	99.20		
3.25	88.50	89.20	90.10	91.10	92.30	93.60	95.00	96.40	97.90	99.30		
3.50	88.60	89.30	90.20	91.30	92.50	93.80	95.20	96.60	98.00	99.50		

3.75	88.70	89.40	90.30	91.40	92.60	93.90	95.30	96.70	98.20	99.60
4.00	88.80	89.60	90.50	91.60	92.80	94.10	95.50	96.90	98.40	99.80
4.25	88.90	89.70	90.70	91.80	93.00	94.30	95.70	97.10	98.60	100.00

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(Continued)

ACCEPTANCE LIMITS FOR DISSOLUTION (Q = 80.0)
 SAMPLING PLAN 2
 LOWER BOUND = 95.0, CONFIDENCE LEVEL = 95.0
 TABLE ENTRIES ARE LOWER LIMITS ON THE MEAN
 OF 60 ASSAYS- 6 ASSAYS AT EACH OF 10 DIFFERENT LOCATIONS
 SE IS THE POOLED WITHIN LOCATION STANDARD DEVIATION
 STANDARD DEVIATIONS AND MEANS ARE EXPRESSED IN % CLAIM

	STANDARD DEVIATION OF LOCATION MEANS											
	4.50	4.75	5.00	5.25	5.50	5.75	6.00	6.25	6.50	6.75	7.00	7.25
SE												
4.50	89.00	89.90	90.80	92.00	93.20	94.60	95.90	97.30	98.80			
4.75	89.20	90.00	91.00	92.20	93.50	94.80	96.20	97.60	99.00			
5.00	89.30	90.20	91.30	92.40	93.70	95.00	96.40	97.80	99.20			
5.25	89.50	90.40	91.50	92.70	94.00	95.30	96.70	98.00	99.50			
5.50	89.70	90.70	91.80	93.00	94.30	95.60	96.90	98.30	99.70			
5.75	90.00	90.90	92.10	93.30	94.50	95.90	97.20	98.60	100.00			
6.00	90.20	91.20	92.40	93.60	94.90	96.20	97.50	98.90				
6.25	90.50	91.60	92.70	93.90	95.20	96.50	97.80	99.20				
6.50	90.80	91.90	93.00	94.30	95.50	96.80	98.10	99.50				
6.75	91.20	92.30	93.40	94.60	95.90	97.20	98.50	99.80				
7.00	91.60	92.60	93.80	95.00	96.20	97.50	98.80					
7.25	92.00	93.10	94.20	95.40	96.60	97.90	99.20					
7.50	92.40	93.50	94.60	95.80	97.00	98.30	99.50					
7.75	92.90	93.90	95.10	96.20	97.40	98.70	99.90					

8.00	93.30	94.40	95.50	96.70	97.80	99.10
8.25	93.80	94.90	96.00	97.10	98.30	99.50
8.50	94.30	95.40	96.50	97.60	98.70	99.90

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(Continued)

OF 60 ASSAYS- 6 ASSAYS AT EACH OF 10 DIFFERENT LOCATIONS
SE IS THE POOLED WITHIN LOCATION STANDARD DEVIATION
STANDARD DEVIATIONS AND MEANS ARE EXPRESSED IN % CLAIM

STANDARD DEVIATION OF LOCATION MEANS

[illegible]

ACCEPTANCE LIMITS FOR DISSOLUTION (Q = 80.0)
 SAMPLING PLAN 2 (10 LOCATIONS, 6 PER LOCATION)
 PROPORTION OF FUTURE SAMPLES PASSING THE USP TEST
 WITH 95.0% ASSURANCE
 GIVEN THE SAMPLE MEAN, WITHIN AND BETWEEN STD DEV

SAMPLE MEAN	SAMPLE WITHIN LOCATION STD DEV	SAMPLE BETWEEN LOCATION STD DEV	LOWER BOUND
100	2.2	2.46	1

ACCEPTANCE LIMITS FOR DISSOLUTION (Q = 80.0)
 SAMPLING PLAN 2
 PROBABILITY OF PASSING DISSOLUTION ACCEPTANCE LIMIT TABLE
 WITH 6 ASSAYS AT EACH OF 10 LOCATIONS
 CONFIDENCE LEVEL = 95.0 & LOWER BOUND = 95.0

Obs	MEAN	WITHIN LOCATION STD DEV	BETWEEN LOCATION STD DEV	PROBABILITY OF PASSING
1	95	2.2	2.2	1.00000
2	100	2.2	2.2	1.00000

ACCEPTANCE LIMITS FOR DISSOLUTION (Q = 80.0)
 SAMPLING PLAN 2
 PROBABILITY OF PASSING DISSOLUTION ACCEPTANCE LIMIT TABLE
 WITH 6 ASSAYS AT EACH OF 10 LOCATIONS
 CONFIDENCE LEVEL = 95.0 & LOWER BOUND = 95.0

Obs	MEAN	WITHIN LOCATION	BETWEEN LOCATION	PROBABILITY
		STD DEV	STD DEV	OF
1	95	2.2	2.2	1.00000
2	100	2.2	2.2	1.00000

ACCEPTANCE LIMITS FOR DISSOLUTION (Q = 80.0)
 SAMPLING PLAN 2 (10 LOCATIONS, 6 PER LOCATION)
 PROPORTION OF FUTURE SAMPLES PASSING THE USP TEST
 WITH 95.0% ASSURANCE
 GIVEN THE SAMPLE MEAN, WITHIN AND BETWEEN STD DEV

SAMPLE MEAN	SAMPLE WITHIN LOCATION STD DEV	SAMPLE BETWEEN LOCATION STD DEV	LOWER BOUND
100	2.2	2.46	1

Appendix

USP Content Uniformity and Dissolution Tests

Content Uniformity

Stage 1) Test 10 dosage units

Requirements are met if the acceptance value (defined below) of the first 10 dosage units is ≤ 15 .

Otherwise go to stage 2.

Stage 2)

Test an additional 20 units.

Pass if for all 30 units the following criteria are met:

The acceptance value of the 30 dosage units is ≤ 15

No dosage unit deviates from the calculated value of M (defined below) by more than 25% of M

The acceptance value (AV) is defined as $|M - \bar{X}| + ks$

Where $k = 2.4$ for stage 1; $k = 2.0$ for stage 2

\bar{X} is the sample mean

s is the standard deviation of the observations.

M is based on T which is the Target content per dosage unit at the time of manufacture, expressed as a percentage of the label claim. Unless otherwise specified in the individual monograph, T is the average of the limits specified in the potency definition in the individual monograph.

M is defined as follows:

When $T \leq 101.5$

Then	$M = \max\{98.5, \bar{X}\}$	if $\bar{X} \leq 100$
	$M = \min\{101.5, \bar{X}\}$	if $\bar{X} > 100$

When $T > 101.5$

Then	$M = \max\{98.5, \bar{X}\}$	if $\bar{X} \leq 100$
	$M = \min\{T, \bar{X}\}$	if $\bar{X} > 100$

Dissolution:

- Stage 1) Test 6 units (Result = % released at specified dissolution time point)
- Pass if all 6 results $\geq Q + 5$
- Otherwise go to stage 2.
- Stage 2) Test 6 additional units
- Pass if for all 12 units the following criteria are met:
- 1) Mean result $\geq Q$
 - 2) No result $\leq Q - 15$
- Otherwise go to stage 3.
- Stage 3) Test 12 additional units
- Pass if for all 24 units the following criteria are met:
- 1) Mean result $\geq Q$
 - 2) No more than two results $\leq Q - 15$ with no results $\leq Q - 25$
- Otherwise Fail.