

Content Uniformity and Dissolution Acceptance Limit Program

USERS GUIDE

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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 its accuracy or use. Any use of the technical documentation or 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 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 two articles contain details on the method with examples. Note: Some methods given in the 1990 article have been revised and are reflected in the current program as well as the 2000 article.

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

Bergum, J. Constructing Acceptance Limits for Multiple Stage Tests. Drug Development & Industrial Pharmacy 16: pp 2153-2166, 1990

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 XXIII 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 XXIII 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 XXIII 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 10 files: Six SAS™ program files (Files.SAS, manager.SAS, Cusp1.SAS, Cusp2.SAS, Disp1.SAS, and Disp2.SAS), an users guide (usersguide.pdf), the validation report (Validation Report.pdf), Acrobat Reader Version 4.0, and a read me text file(readme.txt). The SAS™ programs were written in SAS™ Version 6.12 and will run on any IBM or compatible PC that has SAS 6.12 or later on it. [Note: To run the program in version 8 of SAS, turn off the enhanced editor.]

The Validation Report contains a validation summary, the signed original protocol, amendments, the final amended protocol with signed validation forms, supporting documentation, and validation team curriculum vitas. To navigate the users guide or validation report, use the navigation pane in 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 downloaded to a PC. If the CD drive is not D, then the file Files.SAS must be downloaded and edited to provide the location of the manager macro (manager.SAS) and four analysis macro's (Cusp1.SAS, Cusp2.SAS, Disp1.SAS, and Disp2.SAS). The Files.SAS file is displayed below. Replace the five bolded **D**'s with the location of the programs.

```
**** DIRECTORY FOR MANAGER MACRO *****,
%LET MANAGER = 'D:\MANAGER.SAS';

**** DIRECTORIES FOR ANALYSIS MACROS *****,

%LET CU1 = 'D:\CUSP1.SAS';
%LET CU2 = 'D:\CUSP2.SAS';
%LET DI1 = 'D:\DISP1.SAS';
%LET DI2 = 'D:\DISP2.SAS';

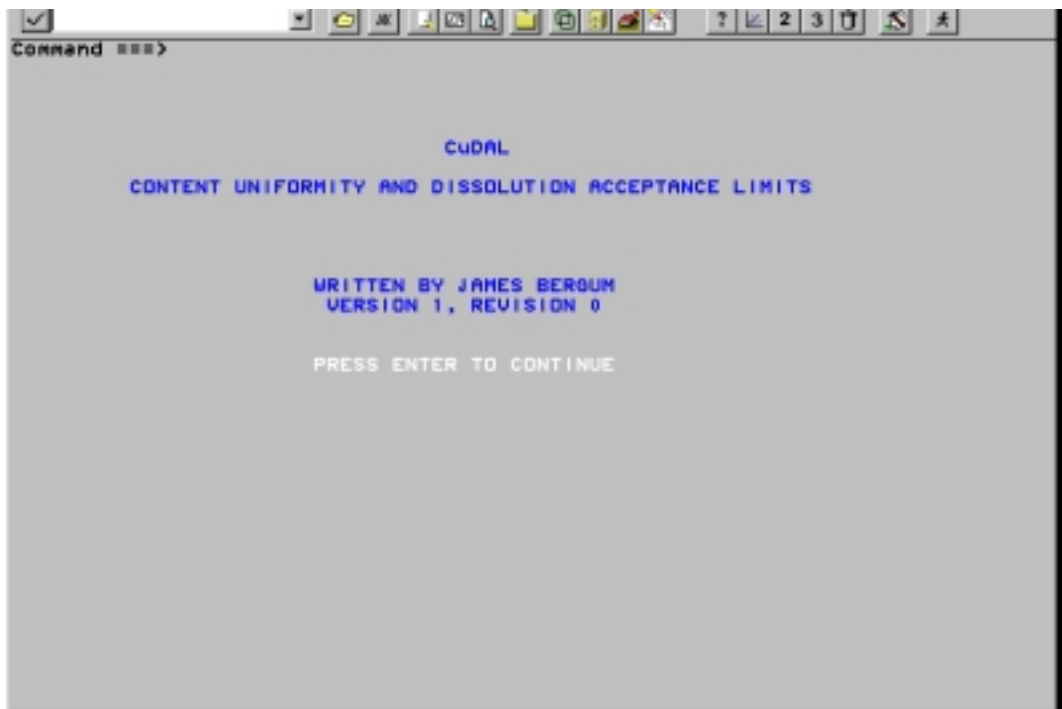
*****.
,

%INCLUDE "&MANAGER";
```

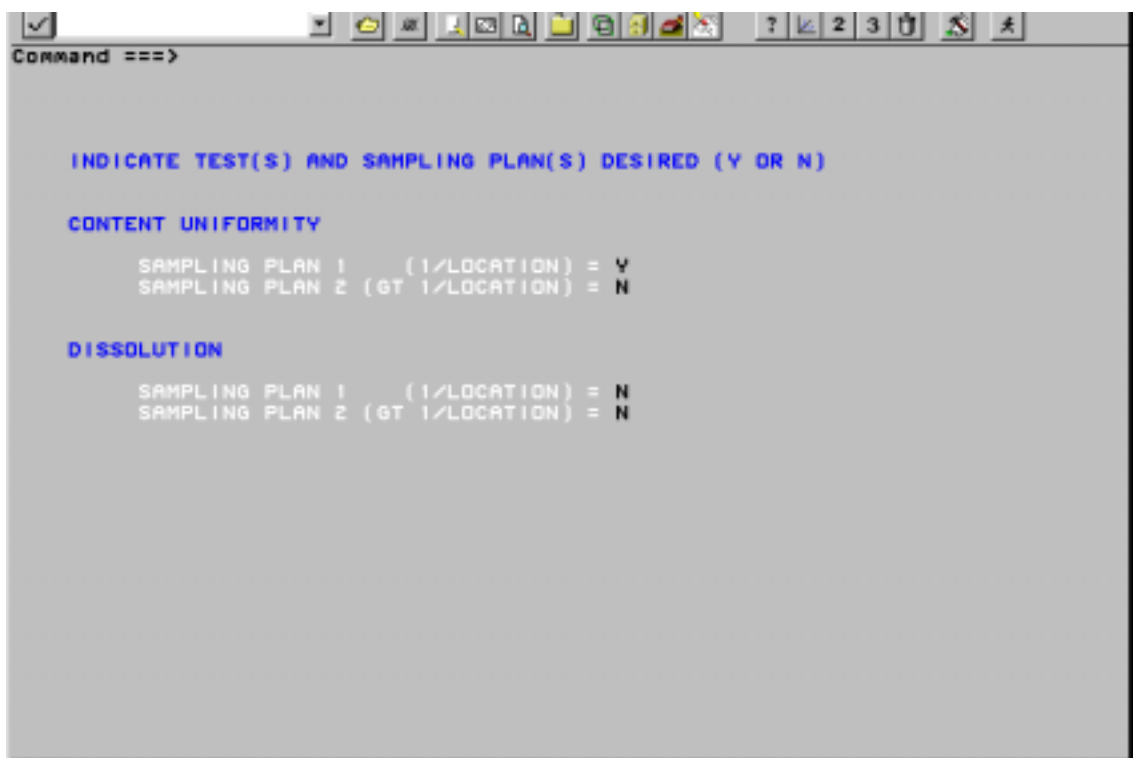
After editing FILES.SAS, the program is ready to submit.

USING THE PROGRAM

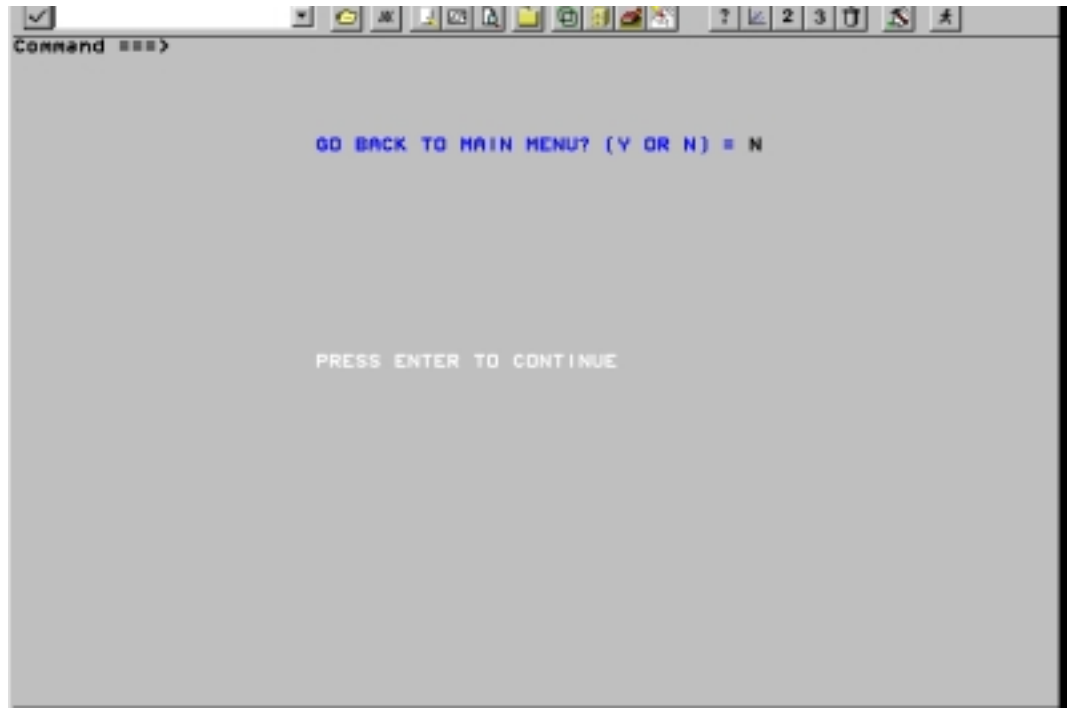
After submitting the file Files.SAS, the following window should appear (If this window does not appear, type NEXT in the SAS command window):



Press enter to continue. The following window will appear:



Indicate by Y or N to select the desired test(s) and sampling plan(s). If all responses are N or once all selected analyses are complete, the following window will appear:



A "Y" response will bring you back to the selection window. An "N" response will exit the program.

Below are the four main screens that will appear depending on the selected analyses. For all four screens, the user inputs the lower bound on the percentage of future samples passing the selected test (P) and the desired confidence level (Q) as well as make a request for printing the acceptance limit table, evaluating the acceptance limit table, and requesting a lower bound for a specific sample result. If a sample is taken from a batch (by either sampling plan 1 or 2) and the results from the tested dosage units pass the acceptance table limits, then the probability that a "future" sample taken from the batch will pass the USP test for content uniformity will be at least P% with Q% assurance. This assumes that the test results from the "future" sample follow sampling plan 1, are independent, and follow a normal distribution.

Content Uniformity (Sampling Plan 1) Main Screen

```
Command ==>
CONTENT UNIFORMITY ACCEPTANCE LIMIT PROGRAM
FOR SAMPLING PLAN 1 (ONE SAMPLE PER LOCATION)

ENTER DOSAGE FORM (TABLET OR CAPSULE):  CAPSULE
ENTER SAMPLE SIZE:  30

ENTER BOUND ON FUTURE PERCENTAGE PASSING (50.0-99.0):  95.0
ENTER CONFIDENCE LEVEL (50.0-99.0):  95.0

DO YOU WANT TO PRINT THE ACCEPTANCE LIMIT TABLE?
ENTER Y OR N =Y

DO YOU WANT TO EVALUATE THE ACCEPTANCE LIMIT TABLE?
ENTER Y OR N =N

DO YOU WANT THE LOWER BOUND FOR A SPECIFIC SAMPLE RESULT?
ENTER Y OR N =N
```

After entering the required information, the program will perform the requested analyses.

Requested Analysis: Print acceptance limit table

The program will send the acceptance limit table to the output window. A typical acceptance limit table is shown below:

ACCEPTANCE LIMITS FOR CAPSULE CONTENT UNIFORMITY(N= 30)
 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	0.04	90.1	2.02	95.1	3.78	100.1	4.61	105.1	3.35	110.1	1.59
85.2	0.08	90.2	2.06	95.2	3.81	100.2	4.62	105.2	3.32	110.2	1.56
85.3	0.13	90.3	2.10	95.3	3.84	100.3	4.62	105.3	3.28	110.3	1.52
85.4	0.17	90.4	2.13	95.4	3.87	100.4	4.62	105.4	3.25	110.4	1.49
85.5	0.21	90.5	2.17	95.5	3.91	100.5	4.62	105.5	3.21	110.5	1.45
85.6	0.25	90.6	2.21	95.6	3.94	100.6	4.63	105.6	3.17	110.6	1.42
85.7	0.29	90.7	2.24	95.7	3.97	100.7	4.63	105.7	3.14	110.7	1.39
85.8	0.33	90.8	2.28	95.8	4.00	100.8	4.63	105.8	3.10	110.8	1.35
85.9	0.37	90.9	2.32	95.9	4.03	100.9	4.63	105.9	3.06	110.9	1.32
86.0	0.42	91.0	2.35	96.0	4.06	101.0	4.63	106.0	3.03	111.0	1.29
86.1	0.46	91.1	2.39	96.1	4.08	101.1	4.63	106.1	2.99	111.1	1.25
86.2	0.50	91.2	2.43	96.2	4.11	101.2	4.62	106.2	2.96	111.2	1.22
86.3	0.54	91.3	2.46	96.3	4.14	101.3	4.60	106.3	2.92	111.3	1.19
86.4	0.58	91.4	2.50	96.4	4.16	101.4	4.57	106.4	2.88	111.4	1.15
86.5	0.62	91.5	2.54	96.5	4.19	101.5	4.55	106.5	2.85	111.5	1.12
86.6	0.66	91.6	2.57	96.6	4.22	101.6	4.53	106.6	2.81	111.6	1.09
86.7	0.70	91.7	2.61	96.7	4.24	101.7	4.50	106.7	2.78	111.7	1.05
86.8	0.74	91.8	2.64	96.8	4.26	101.8	4.48	106.8	2.74	111.8	1.02
86.9	0.78	91.9	2.68	96.9	4.28	101.9	4.45	106.9	2.70	111.9	0.99
87.0	0.82	92.0	2.72	97.0	4.31	102.0	4.42	107.0	2.67	112.0	0.96
87.1	0.86	92.1	2.75	97.1	4.33	102.1	4.40	107.1	2.63	112.1	0.92
87.2	0.90	92.2	2.79	97.2	4.35	102.2	4.37	107.2	2.60	112.2	0.89
87.3	0.94	92.3	2.82	97.3	4.36	102.3	4.34	107.3	2.56	112.3	0.86
87.4	0.98	92.4	2.86	97.4	4.38	102.4	4.31	107.4	2.53	112.4	0.83
87.5	1.02	92.5	2.90	97.5	4.40	102.5	4.27	107.5	2.49	112.5	0.79
87.6	1.06	92.6	2.93	97.6	4.41	102.6	4.24	107.6	2.46	112.6	0.76
87.7	1.10	92.7	2.97	97.7	4.43	102.7	4.21	107.7	2.42	112.7	0.73
87.8	1.14	92.8	3.00	97.8	4.44	102.8	4.18	107.8	2.38	112.8	0.70
87.9	1.18	92.9	3.04	97.9	4.46	102.9	4.14	107.9	2.35	112.9	0.66
88.0	1.22	93.0	3.07	98.0	4.47	103.0	4.11	108.0	2.31	113.0	0.63
88.1	1.26	93.1	3.11	98.1	4.48	103.1	4.07	108.1	2.28	113.1	0.60
88.2	1.29	93.2	3.14	98.2	4.49	103.2	4.04	108.2	2.24	113.2	0.57
88.3	1.33	93.3	3.17	98.3	4.50	103.3	4.00	108.3	2.21	113.3	0.54
88.4	1.37	93.4	3.21	98.4	4.51	103.4	3.97	108.4	2.17	113.4	0.50
88.5	1.41	93.5	3.24	98.5	4.52	103.5	3.93	108.5	2.14	113.5	0.47
88.6	1.45	93.6	3.28	98.6	4.53	103.6	3.90	108.6	2.10	113.6	0.44
88.7	1.49	93.7	3.31	98.7	4.54	103.7	3.86	108.7	2.07	113.7	0.41
88.8	1.53	93.8	3.35	98.8	4.55	103.8	3.82	108.8	2.03	113.8	0.38
88.9	1.57	93.9	3.38	98.9	4.56	103.9	3.79	108.9	2.00	113.9	0.34
89.0	1.60	94.0	3.41	99.0	4.56	104.0	3.75	109.0	1.97	114.0	0.31
89.1	1.64	94.1	3.45	99.1	4.57	104.1	3.72	109.1	1.93	114.1	0.28
89.2	1.68	94.2	3.48	99.2	4.58	104.2	3.68	109.2	1.90	114.2	0.25
89.3	1.72	94.3	3.52	99.3	4.58	104.3	3.64	109.3	1.86	114.3	0.22
89.4	1.76	94.4	3.55	99.4	4.59	104.4	3.61	109.4	1.83	114.4	0.19
89.5	1.80	94.5	3.58	99.5	4.59	104.5	3.57	109.5	1.79	114.5	0.16
89.6	1.83	94.6	3.62	99.6	4.60	104.6	3.54	109.6	1.76	114.6	0.12
89.7	1.87	94.7	3.65	99.7	4.60	104.7	3.50	109.7	1.73	114.7	0.09
89.8	1.91	94.8	3.68	99.8	4.60	104.8	3.46	109.8	1.69	114.8	0.06
89.9	1.95	94.9	3.71	99.9	4.61	104.9	3.43	109.9	1.66	114.9	0.03
90.0	1.98	95.0	3.75	100.0	4.61	105.0	3.39	110.0	1.62		

To use the acceptance table for sampling plan 1, the sample mean and sample coefficient of variation (cv) is computed from the n test results. Express both statistics as a percent of label claim. Then look up the mean in the acceptance table corresponding to the calculated sample mean (round to the mean with the smallest corresponding cv entry). If the corresponding cv entry is greater than the computed sample cv, the sample passes the acceptance limits.

In the acceptance limit table shown above, a sample mean of 98.6% label claim must have a sample cv less than 4.53% to pass.

Requested Analysis: Evaluate an acceptance limit table

Once a table has been generated, it should be examined for its ability to pass a "good" batch and fail a "bad" batch. This can be done by specifying a population value for the mean and cv, and then calculating the probability of passing the acceptance limit table. So suppose that the population mean is 100 and the population cv is 2.0%. This might be considered a "good" underlying population (The 2.0% cv might be based on some other data such as the assay validation results for precision.) The evaluation program determines the probability that a sample result will pass the acceptance limit table for this "good" population. If the probability is low, say less than 90%, then one way to increase the probability is to increase the sample size. Therefore, choose a larger sample size and evaluate again. Now pick a "bad" underlying population such as a mean of 90% and a cv of 2.0%. The probability for passing the acceptance limit table should be low. If not, a larger sample size should be considered.

If the evaluation is requested, the following window will appear:

```
Command ==>
CONTENT UNIFORMITY ACCEPTANCE LIMIT PROGRAM
FOR SAMPLING PLAN 1 (ONE SAMPLE PER LOCATION)

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
```

The window requests the upper and lower bounds for the mean and cv, the increment, and the divisor. All entrees must be integer. So, the default screen shown above will determine the

probability of passing an acceptance limit table for population means of 95.0 (950/10) and 100.0 (1000/10) with cvs of 1.0 (10/10) and 4.0 (40/10)%.

Typical output is displayed below:

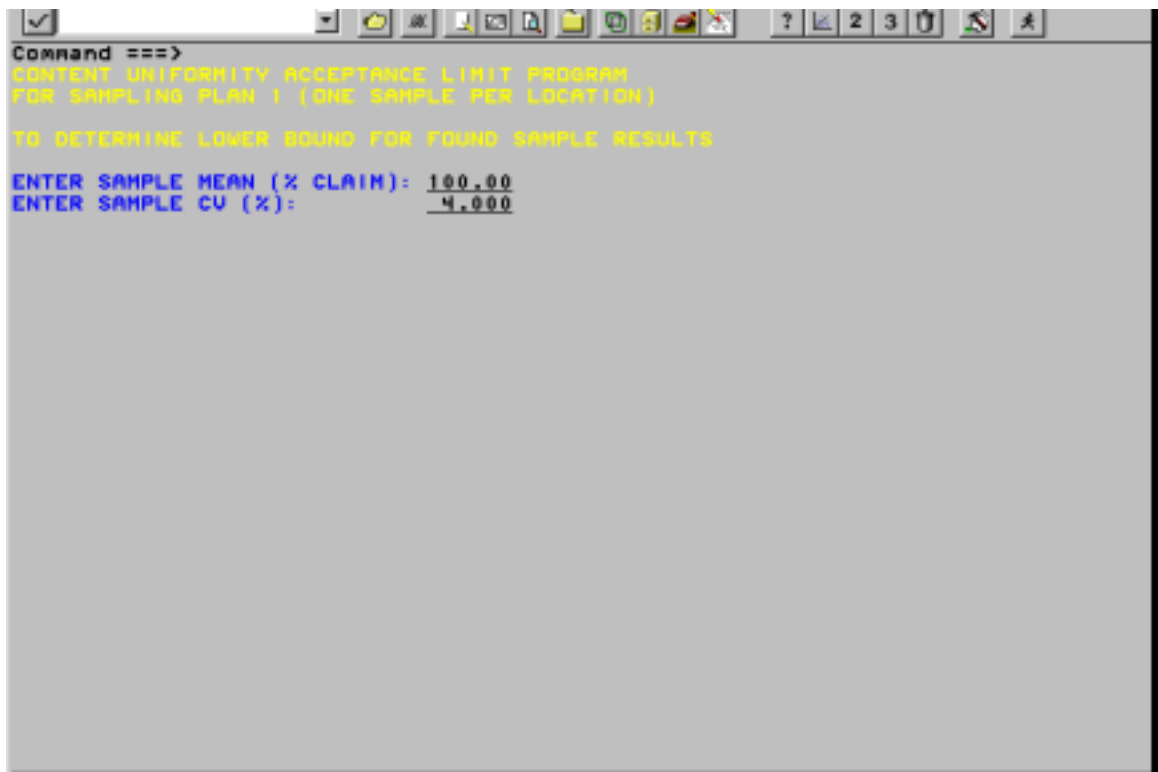
ACCEPTANCE LIMIT TABLE FOR CAPSULE CONTENT UNIFORMITY (N=30)
SAMPLING PLAN 1
DETERMINE PROBABILITY OF PASSING ACCEPTANCE LIMIT TABLE
CONFIDENCE LEVEL = 95.0 AND LOWER BOUND = 95.0

U	CV	PROBABILITY
		OF PASSING
95	1	1.00000
100	1	1.00000
95	4	0.35602
100	4	0.88358

If the population mean and cv are 100 and 4% respectively, then the probability of passing the acceptance limit table for capsule content uniformity is 0.88358 (88.3%).

Requested Analysis: Find Lower Bound for Sample Results

If the request is for a lower bound on the proportion of future samples passing the test, then the following window will appear. Note: The lower bound given in the main window is ignored for this analysis since the purpose of this analysis is to calculate the lower bound.



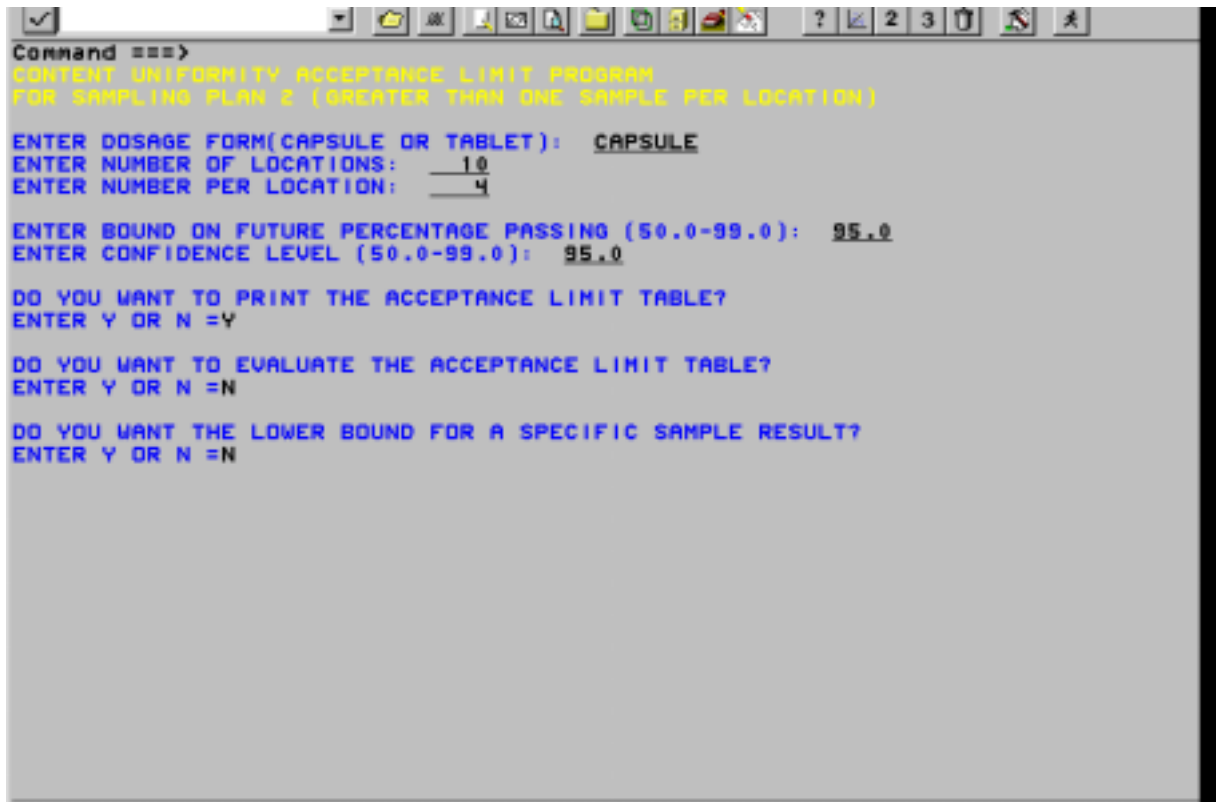
After inputting the sample mean and cv (both as % label claim), the program will provide the following output:

ACCEPTANCE LIMIT TABLE FOR CAPSULE 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	0.99850

For a sample of 30 capsules with a sample mean of 100 and cv of 4.0%, there is at least a 99.85% chance that a sample tested for content uniformity will pass the USP content uniformity test.

Content Uniformity (Sampling Plan 2) Main Screen



The screenshot shows a command-line interface for a program titled "CONTENT UNIFORMITY ACCEPTANCE LIMIT PROGRAM FOR SAMPLING PLAN 2 (GREATER THAN ONE SAMPLE PER LOCATION)". The interface is displayed in a window with a standard toolbar at the top. The text is as follows:

```
Command ===>
CONTENT UNIFORMITY ACCEPTANCE LIMIT PROGRAM
FOR SAMPLING PLAN 2 (GREATER THAN ONE SAMPLE PER LOCATION)

ENTER DOSAGE FORM(CAPSULE OR TABLET):  CAPSULE
ENTER NUMBER OF LOCATIONS:      10
ENTER NUMBER PER LOCATION:      4

ENTER BOUND ON FUTURE PERCENTAGE PASSING (50.0-99.0):  95.0
ENTER CONFIDENCE LEVEL (50.0-99.0):  95.0

DO YOU WANT TO PRINT THE ACCEPTANCE LIMIT TABLE?
ENTER Y OR N =Y

DO YOU WANT TO EVALUATE THE ACCEPTANCE LIMIT TABLE?
ENTER Y OR N =N

DO YOU WANT THE LOWER BOUND FOR A SPECIFIC SAMPLE RESULT?
ENTER Y OR N =N
```

After entering the required information, the program will perform the requested analyses.

Requested Analysis: Print acceptance limit table

The program will output the acceptance limit table to the output window. A typical page from an acceptance limit table is as follows:

ACCEPTANCE LIMITS FOR CAPSULE CONTENT UNIFORMITY
SAMPLING PLAN 2
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	85.5	114.5	85.9	114.1	86.4	113.6	86.8	113.2	87.2	112.8	87.7	112.3	88.1	111.9	88.5	111.5	89.0	111.0
0.2	85.6	114.4	86.0	114.0	86.4	113.6	86.8	113.2	87.2	112.8	87.7	112.3	88.1	111.9	88.5	111.5	89.0	111.0
0.3	85.8	114.2	86.1	113.9	86.5	113.5	86.9	113.1	87.3	112.7	87.7	112.3	88.1	111.9	88.6	111.4	89.0	111.0
0.4	86.0	114.0	86.2	113.8	86.5	113.5	86.9	113.1	87.3	112.7	87.7	112.3	88.2	111.8	88.6	111.4	89.0	111.0
0.5	86.2	113.8	86.4	113.6	86.7	113.3	87.0	113.0	87.4	112.6	87.8	112.2	88.2	111.8	88.6	111.4	89.1	110.9
0.6	86.4	113.6	86.5	113.5	86.8	113.2	87.1	112.9	87.5	112.5	87.9	112.1	88.3	111.7	88.7	111.3	89.1	110.9
0.7	86.5	113.5	86.7	113.3	86.9	113.1	87.2	112.8	87.6	112.4	88.0	112.0	88.3	111.7	88.7	111.3	89.2	110.8
0.8	86.7	113.3	86.9	113.1	87.1	112.9	87.4	112.6	87.7	112.3	88.0	112.0	88.4	111.6	88.8	111.2	89.2	110.8
0.9	86.9	113.1	87.1	112.9	87.3	112.7	87.5	112.5	87.8	112.2	88.2	111.8	88.5	111.5	88.9	111.1	89.3	110.7
1.0	87.1	112.9	87.3	112.7	87.5	112.5	87.7	112.3	88.0	112.0	88.3	111.7	88.6	111.4	89.0	111.0	89.4	110.6
1.1	87.3	112.7	87.5	112.5	87.6	112.4	87.9	112.1	88.1	111.9	88.4	111.6	88.7	111.3	89.1	110.9	89.4	110.6
1.2	87.5	112.5	87.7	112.3	87.8	112.2	88.0	112.0	88.3	111.7	88.5	111.5	88.8	111.2	89.2	110.8	89.5	110.5
1.3	87.7	112.3	87.9	112.1	88.0	112.0	88.2	111.8	88.4	111.6	88.7	111.3	89.0	111.0	89.3	110.7	89.6	110.4
1.4	87.9	112.1	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
1.5	88.1	111.9	88.2	111.8	88.4	111.6	88.6	111.4	88.8	111.2	89.0	111.0	89.3	110.7	89.6	110.4	89.9	110.1
1.6	88.3	111.7	88.4	111.6	88.6	111.4	88.8	111.2	89.0	111.0	89.2	110.8	89.4	110.6	89.7	110.3	90.0	110.0
1.7	88.5	111.5	88.6	111.4	88.8	111.2	88.9	111.1	89.1	110.9	89.3	110.7	89.6	110.4	89.9	110.1	90.1	109.9
1.8	88.7	111.3	88.8	111.2	89.0	111.0	89.1	110.9	89.3	110.7	89.5	110.5	89.8	110.2	90.0	110.0	90.3	109.7
1.9	88.9	111.1	89.0	111.0	89.2	110.8	89.3	110.7	89.5	110.5	89.7	110.3	89.9	110.1	90.2	109.8	90.4	109.6
2.0	89.1	110.9	89.2	110.8	89.3	110.7	89.5	110.5	89.7	110.3	89.9	110.1	90.1	109.9	90.3	109.7	90.6	109.4
2.1	89.3	110.7	89.4	110.6	89.5	110.5	89.7	110.3	89.9	110.1	90.1	109.9	90.3	109.7	90.5	109.5	90.7	109.3
2.2	89.4	110.6	89.6	110.4	89.7	110.3	89.9	110.1	90.1	109.9	90.2	109.8	90.4	109.6	90.7	109.3	90.9	109.1
2.3	89.6	110.4	89.8	110.2	89.9	110.1	90.1	109.9	90.2	109.8	90.4	109.6	90.6	109.4	90.8	109.2	91.1	108.9
2.4	89.8	110.2	90.0	110.0	90.1	109.9	90.3	109.7	90.4	109.6	90.6	109.4	90.8	109.2	91.0	109.0	91.2	108.8
2.5	90.0	110.0	90.2	109.8	90.3	109.7	90.5	109.5	90.6	109.4	90.8	109.2	91.0	109.0	91.2	108.8	91.4	108.6
2.6	90.2	109.8	90.4	109.6	90.5	109.5	90.7	109.3	90.8	109.2	91.0	109.0	91.2	108.8	91.4	108.6	91.6	108.4
2.7	90.4	109.6	90.6	109.4	90.7	109.3	90.8	109.2	91.0	109.0	91.2	108.8	91.4	108.6	91.5	108.5	91.8	108.2
2.8	90.6	109.4	90.7	109.3	90.9	109.1	91.0	109.0	91.2	108.8	91.4	108.6	91.5	108.5	91.7	108.3	91.9	108.1
2.9	90.8	109.2	90.9	109.1	91.1	108.9	91.2	108.8	91.4	108.6	91.6	108.4	91.7	108.3	91.9	108.1	92.1	107.9
3.0	91.0	109.0	91.1	108.9	91.3	108.7	91.4	108.6	91.6	108.4	91.7	108.3	91.9	108.1	92.1	107.9	92.3	107.7
3.1	91.2	108.8	91.3	108.7	91.5	108.5	91.6	108.4	91.8	108.2	91.9	108.1	92.1	107.9	92.3	107.7	92.5	107.5
3.2	91.4	108.6	91.5	108.5	91.7	108.3	91.8	108.2	92.0	108.0	92.1	107.9	92.3	107.7	92.5	107.5	92.7	107.3
3.3	91.6	108.4	91.7	108.3	91.9	108.1	92.0	108.0	92.2	107.8	92.3	107.7	92.5	107.5	92.7	107.3	92.8	107.2
3.4	91.8	108.2	91.9	108.1	92.1	107.9	92.2	107.8	92.3	107.7	92.5	107.5	92.7	107.3	92.8	107.2	93.0	107.0
3.5	92.0	108.0	92.1	107.9	92.2	107.8	92.4	107.6	92.5	107.5	92.7	107.3	92.9	107.1	93.0	107.0	93.2	106.8
3.6	92.2	107.8	92.3	107.7	92.4	107.6	92.6	107.4	92.7	107.3	92.9	107.1	93.1	106.9	93.2	106.8	93.4	106.6
3.7	92.4	107.6	92.5	107.5	92.6	107.4	92.8	107.2	92.9	107.1	93.1	106.9	93.2	106.8	93.4	106.6	93.6	106.4
3.8	92.6	107.4	92.7	107.3	92.8	107.2	93.0	107.0	93.1	106.9	93.3	106.7	93.4	106.6	93.6	106.4	93.8	106.2
3.9	92.8	107.2	92.9	107.1	93.0	107.0	93.2	106.8	93.3	106.7	93.5	106.5	93.6	106.4	93.8	106.2	94.0	106.0
4.0	93.0	107.0	93.1	106.9	93.2	106.8	93.4	106.6	93.5	106.5	93.7	106.3	93.8	106.2	94.0	106.0	94.2	105.8
4.1	93.2	106.8	93.3	106.7	93.4	106.6	93.6	106.4	93.7	106.3	93.9	106.1	94.0	106.0	94.2	105.8	94.4	105.6
4.2	93.4	106.6	93.5	106.5	93.6	106.4	93.8	106.2	93.9	106.1	94.1	105.9	94.2	105.8	94.4	105.6	94.6	105.4
4.3	93.6	106.4	93.7	106.3	93.8	106.2	94.0	106.0	94.1	105.9	94.3	105.7	94.4	105.6	94.6	105.4	94.8	105.2

To use sampling plan 2, calculate the within location standard deviation (SE), the standard deviation of the location means (SM), and the overall mean as follows: Suppose there are n results (expressed in % label claim) from each of L locations. For each location, calculate the sample mean and sample variance. The square root of the average of the L sample variances is SE. The standard deviation of the L sample means is SM. Note: This is not the variance component. The mean of the L means is the overall mean.

The sample meets the acceptance limits if the overall mean of the sample falls within the limits corresponding to the appropriate SE and SM value (Round the calculated SE and SM up when using the table).

In the sample page given above, if the sample standard deviation of the location means (after rounding up to the nearest tenth) is 0.4 and SE is 2.0 (after rounding up), then the overall sample mean must be between 89.5% and 110.5% of label claim.

Requested Analysis: Evaluate an acceptance limit table

The following window will appear:

```
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
```

The user specifies the range of possible population values for the mean, within location standard deviation, and between location standard deviation. Note: The between location standard deviation is the between location variance component and not the standard deviation of the location means used in the acceptance limit table. For the population mean, the user specifies the lower bound for the mean, the upper bound for the mean, the increment, and the divisor. Each of these values must be a positive integer. The default screen given above evaluates the

population means of 95.0 (950/10) and 100.0 (1000/10), within standard deviation of 2.2 (22/10)%, and between location standard deviation of 2.2 (22/10)%.

Typical results for the evaluation are given below:

ACCEPTANCE LIMITS FOR CAPSULE 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	0.28601
2	100	2.2	2.2	0.84638

If the population mean, within location standard deviation, and between location standard deviation are 95% of claim and 2.2%, and 2.2%, respectively, then the probability of a sample consisting of 40 capsules (4 from each of 10 locations) passing the acceptance limit table is 0.28601 (28.6%).

Requested Analysis: Find Lower Bound

This is used to calculate the lower bound on the proportion of future samples passing the USP content uniformity test given the sample mean, sample within location standard deviation, and the standard deviation of location means (Note: This is not the variance component for between location.). The user inputs the sample mean, sample within location standard deviation, and standard deviation of location means. Note: The lower bound given in the main window is ignored for this analysis since the purpose of this analysis is to calculate the lower bound. The following window will appear:

Command ===>

TO DETERMINE LOWER BOUND FOR FOUND SAMPLE RESULTS

ENTER SAMPLE MEAN (% CLAIM): 100.00

ENTER SAMPLE WITHIN STD DEV (% CLAIM): 2.200

ENTER SAMPLE BETWEEN STD DEV (% CLAIM): 2.460
(I.E. STANDARD DEVIATION OF SAMPLE LOCATION MEANS)

Enter the within location standard deviation (SE), the standard deviation of the location means (SM), and the overall mean from your sample based on the following calculations: Suppose there are n results (expressed in % label claim) from each of L locations. For each location, calculate the sample mean and sample variance. The square root of the average of the L sample variances is SE. The standard deviation of the L sample means is SM. Note: This is not the variance component. The mean of the L means is the overall mean.

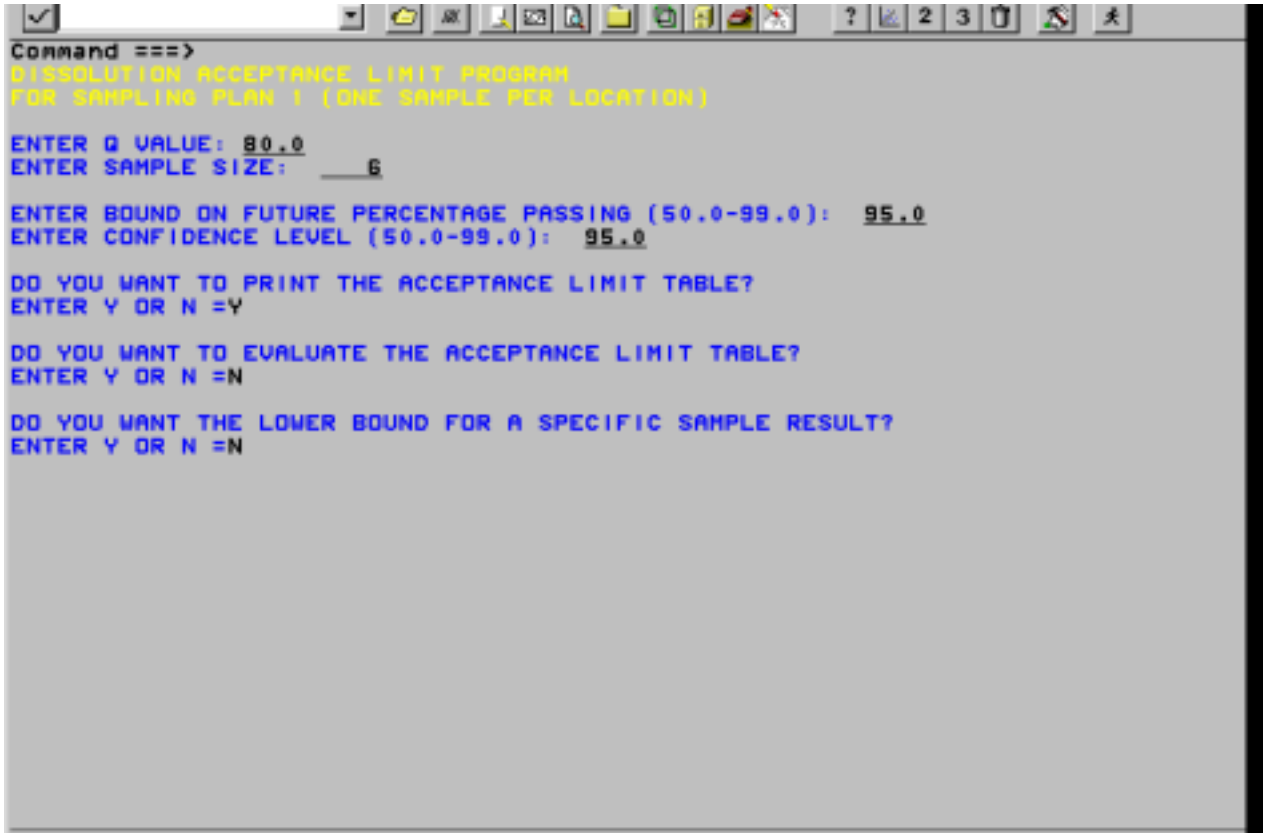
After entering a sample mean, within location standard deviation (SE), and between location standard deviation (SM), typical results are given below:

ACCEPTANCE LIMITS FOR CAPSULE 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	0.99973

Based on the a sample mean, within location standard deviation, and between location standard deviation of 100%, 2.2%, and 2.46% based on a sample of 40 capsule results (4 from each of 10 locations), there is at least a 99.97% chance that a sample tested for content uniformity will pass the USP test.

Dissolution (Sampling Plan 1) Main Screen



```
Command ==>
DISSOLUTION ACCEPTANCE LIMIT PROGRAM
FOR SAMPLING PLAN 1 (ONE SAMPLE PER LOCATION)

ENTER Q VALUE: 80.0
ENTER SAMPLE SIZE: 6

ENTER BOUND ON FUTURE PERCENTAGE PASSING (50.0-99.0): 95.0
ENTER CONFIDENCE LEVEL (50.0-99.0): 95.0

DO YOU WANT TO PRINT THE ACCEPTANCE LIMIT TABLE?
ENTER Y OR N =Y

DO YOU WANT TO EVALUATE THE ACCEPTANCE LIMIT TABLE?
ENTER Y OR N =N

DO YOU WANT THE LOWER BOUND FOR A SPECIFIC SAMPLE RESULT?
ENTER Y OR N =N
```

After entering the required information, the program will perform the requested analyses.

Requested Analysis: Print acceptance limit table

The program will send the acceptance limit table to the output window. A typical page from an acceptance limit table is shown below:

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

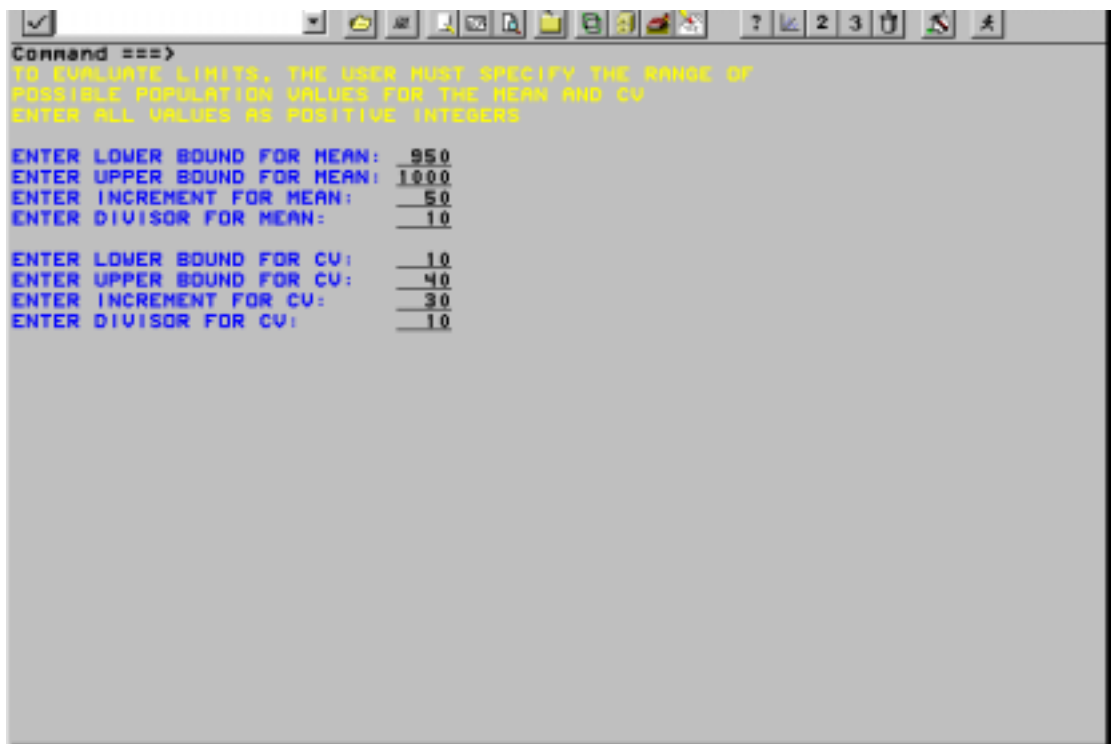
MEAN (% CLAIM)	CV (%)	MEAN (% CLAIM)	CV (%)	MEAN (% CLAIM)	CV (%)	MEAN (% CLAIM)	CV (%)	MEAN (% CLAIM)	CV (%)
80.2	0.09	84.2	1.80	88.2	3.34	92.2	4.28	96.2	4.69
80.4	0.18	84.4	1.88	88.4	3.41	92.4	4.31	96.4	4.70
80.6	0.27	84.6	1.96	88.6	3.47	92.6	4.33	96.6	4.72
80.8	0.36	84.8	2.04	88.8	3.54	92.8	4.36	96.8	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

To use the acceptance table for sampling plan 1, the sample mean and sample coefficient of variation (cv) is computed from the n test results. Express both statistics as a percent of label claim. Then look up the mean in the acceptance table corresponding to the calculated sample mean (round to the mean with the smallest corresponding cv entry). If the corresponding cv entry is greater than the computed sample cv, the sample passes the acceptance limits.

In the table above, a sample mean of 89.8% released requires a cv less than 3.82%.

Requested Analysis: Evaluate an acceptance limit table

Once a table has been generated, it should be examined for its ability to pass a "good" batch and fail a "bad" batch. This can be done by specifying a population value for the mean and cv, and then calculating the probability of passing the acceptance limit table. If the evaluation is requested, the following window will appear:



The screenshot shows a command window with a title bar containing standard icons. The text inside the window is as follows:

```
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
```

The window requests the upper and lower bounds for the mean and cv, the increment, and the divisor. All entrees must be integer. So, the default screen shown above will determine the probability of passing an acceptance limit table for population means of 95.0 (950/10) and 100.0 (1000/10) with cvs of 1.0 (10/10) and 4.0 (40/10)%.

Typical output is displayed below:

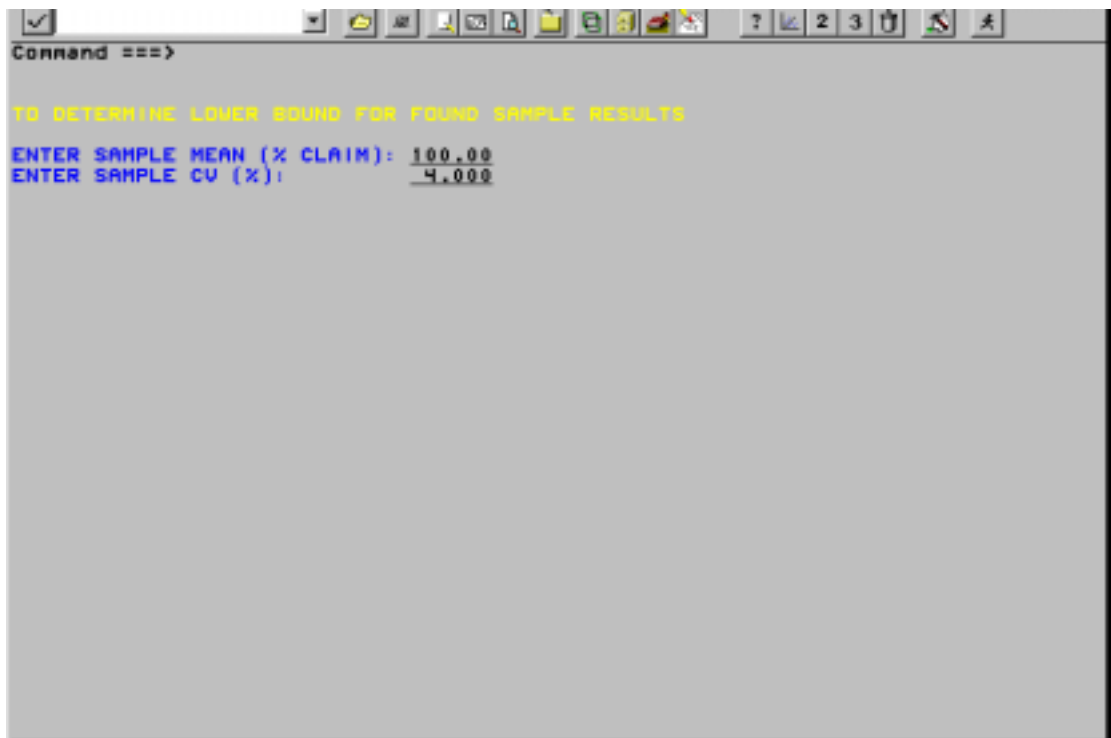
ACCEPTANCE LIMITS FOR DISSOLUTION (N = 6, Q = 80.0)
SAMPLING PLAN 1
PROBABILITY OF PASSING ACCEPTANCE LIMIT TABLE
CONFIDENCE LEVEL = 95.0 AND LOWER BOUND = 95.0

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

If the population mean and cv are 95% and 4%, respectively, then the probability of a sample of 6 dosage units passing the acceptance limit table is 0.7398 (73.98%).

Requested Analysis: Find Lower Bound for Sample Results

The following window will appear. Note: The lower bound given in the main window is ignored for this analysis since the purpose of this analysis is to calculate the lower bound.



The screenshot shows a software window with a title bar containing a checkmark icon and a menu bar with icons for file operations and help. The main area of the window has a light gray background. At the top, it says "Command ==>". Below this, there is a yellow text prompt: "TO DETERMINE LOWER BOUND FOR FOUND SAMPLE RESULTS". Underneath, there are two input fields: "ENTER SAMPLE MEAN (% CLAIM):" followed by the value "100.00" and "ENTER SAMPLE CV (%):" followed by the value "4.000".

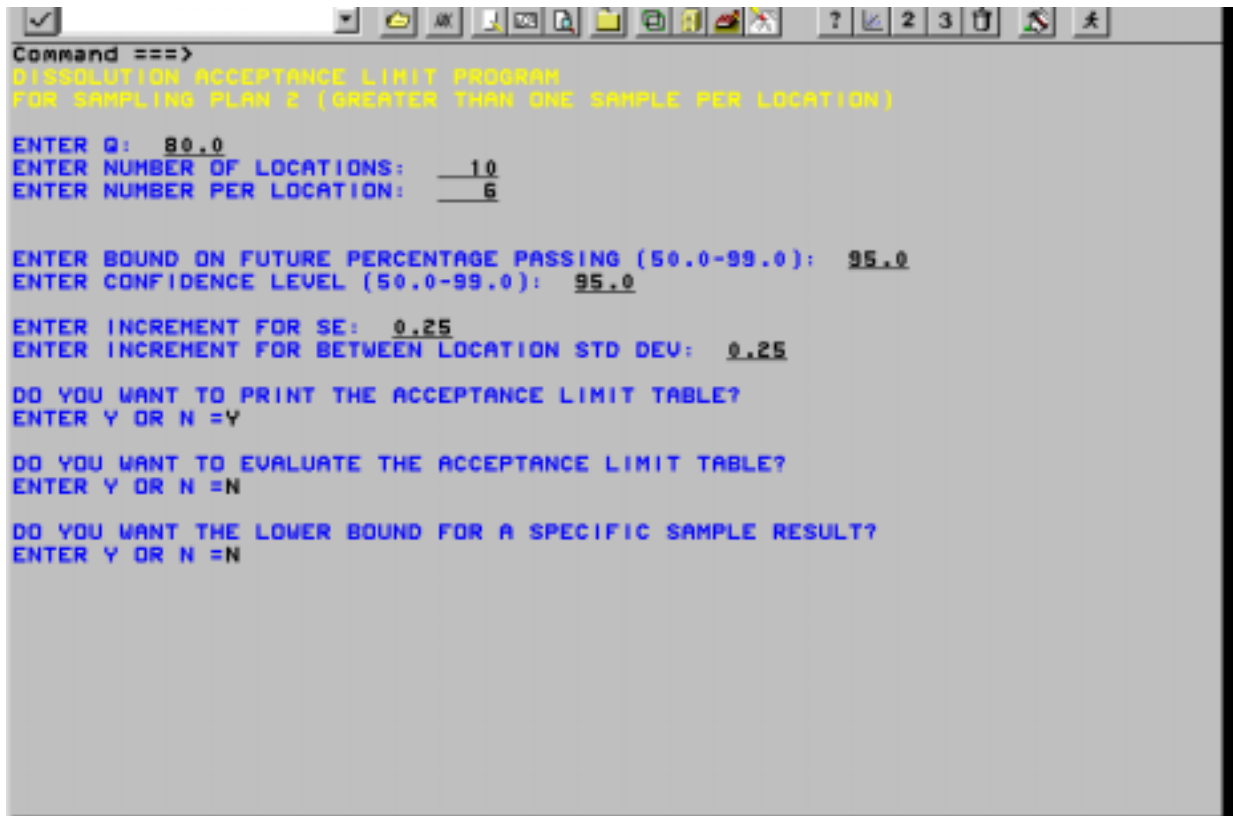
After inputting the sample mean and cv (both as % label claim), the program will provide the following output:

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

If the sample mean is 100% claim with a sample cv of 4%, the there is at least a 99.8% chance that a future sample will pass the USP dissolution test.

Dissolution (Sampling Plan 2) Main Screen



The screenshot shows a software window titled "Dissolution Acceptance Limit Program" with a menu bar and a toolbar. The main text area contains the following prompts and user inputs:

```
Command ==>
DISSOLUTION ACCEPTANCE LIMIT PROGRAM
FOR SAMPLING PLAN 2 (GREATER THAN ONE SAMPLE PER LOCATION)

ENTER Q: 80.0
ENTER NUMBER OF LOCATIONS: 10
ENTER NUMBER PER LOCATION: 6

ENTER BOUND ON FUTURE PERCENTAGE PASSING (50.0-99.0): 95.0
ENTER CONFIDENCE LEVEL (50.0-99.0): 95.0

ENTER INCREMENT FOR SE: 0.25
ENTER INCREMENT FOR BETWEEN LOCATION STD DEV: 0.25

DO YOU WANT TO PRINT THE ACCEPTANCE LIMIT TABLE?
ENTER Y OR N =Y

DO YOU WANT TO EVALUATE THE ACCEPTANCE LIMIT TABLE?
ENTER Y OR N =N

DO YOU WANT THE LOWER BOUND FOR A SPECIFIC SAMPLE RESULT?
ENTER Y OR N =N
```

After entering the required information, the program will perform the requested analyses.

Requested Analysis: Print acceptance limit table

The program will output the acceptance limit table to the output window. A typical page from an acceptance limit table is as follows:

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																	
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
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

(CONTINUED)

To use sampling plan 2, calculate the within location standard deviation (SE), the standard deviation of the location means (SM), and the overall mean as follows: Suppose there are n results (expressed in % label claim) from each of L locations. For each location, calculate the sample mean and sample variance. The square root of the average of the L sample variances is SE. The standard deviation of the L sample means is SM. Note: This is not the variance component. The mean of the L means is the overall mean.

The sample meets the acceptance limits if the overall mean of the sample falls within the limits corresponding to the appropriate SE and SM value (Round the calculated SE and SM up when using the table).

In the table given above, if the standard deviation of location means is 2.00% released (after rounding up to the nearest 0.25%) and SE is 3.25% (after rounding), then the overall sample mean must be less than 83.90% to pass.

Requested Analysis: Evaluate an acceptance limit table

If the evaluation is requested, the following window will appear:

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

The user specifies the range of possible population values for the mean, within location standard deviation, and between location standard deviation. Note: The between location standard deviation is the between location variance component and not the standard deviation of the location means used in the acceptance limit table. For the population mean, the user specifies the lower bound for the mean, the upper bound for the mean, the increment, and the divisor. Each of these values must be a positive integer. The default screen given above evaluates the population means of 95.0 (950/10) and 100.0 (1000/10), within standard deviation of 2.2 (22/10)%, and between location standard deviation of 2.2 (22/10)%.

Typical results for the evaluation are given below:

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	85	2.2	2.2	0.68164
2	85	2.7	2.2	0.61109
3	85	3.2	2.2	0.53105
4	90	2.2	2.2	0.99996
5	90	2.7	2.2	0.99987
6	90	3.2	2.2	0.99956

If the population mean is 85% released with a within location standard deviation of 3.2 and a between location standard deviation of 2.2, then there is a 53.1% chance of passing the acceptance limit table associated with a sampling plan of 6 dosage units at each of 10 locations.

Requested Analysis: Find Lower Bound

This is used to calculate the lower bound on the proportion of future samples passing the USP content uniformity test given the sample mean, sample within location standard deviation, and the standard deviation of location means (Note: This is not the variance component for between location.). The user inputs the sample mean, sample within location standard deviation, and standard deviation of location means. Note: The lower bound given in the main window is ignored for this analysis since the purpose of this analysis is to calculate the lower bound. If the request is for a lower bound on the proportion of future samples passing the test, the following window will appear:


```

Command ==>

TO DETERMINE LOWER BOUND FOR FOUND SAMPLE RESULTS

ENTER SAMPLE MEAN (% CLAIM):      100.00
ENTER SAMPLE WITHIN STD DEV (% CLAIM):  2.200
ENTER SAMPLE BETWEEN STD DEV (% CLAIM): 2.460
(I.E. STANDARD DEVIATION OF SAMPLE LOCATION MEANS)
  
```

Enter the within location standard deviation (SE), the standard deviation of the location means (SM), and the overall mean from your sample based on the following calculations: Suppose there are n results (expressed in % label claim) from each of L locations. For each location, calculate the sample mean and sample variance. The square root of the average of the L sample variances is SE. The standard deviation of the L sample means is SM. Note: This is not the variance component. The mean of the L means is the overall mean.

After inputting the sample mean, within location standard deviation, and between location standard deviation, typical results are given below:

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
85	2.2	2.46	0.98664

Based on a sample mean of 85% with a sample within location standard deviation of 2.2% and between location standard deviation of 2.46%, there is at least a 98.6% chance that a future sample will pass the USP dissolution test.

Appendix USP XXIII Tests

Content Uniformity for Tablets:

- Stage 1) Test 10 units.
- Pass if following criteria are met:
- 1) $CV \leq 6.0\%$
 - 2) No value is outside 85% to 115% of Claim
- Stage 2) Test 20 additional units.
- Pass if for all 30 units the following criteria are met:
- 1) $CV \leq 7.8\%$
 - 2) No more than one value is outside 85% to 115% of claim and no value is outside 75% to 125% of claim.

Content Uniformity For Capsules

- Stage 1) Test 10 units.
- Pass if the following criteria are met:
- 1) $CV \leq 6.0\%$
 - 2) No more than one value outside 85% to 115% of Claim with no value outside 75% to 125% of claim
- Stage 2) Test 20 additional units.
- Pass if for all 30 units the following criteria are met:
- 1) $CV \leq 7.8\%$
 - 2) No more than three values are outside 85% to 115% of claim and no value is outside 75% to 125% of claim.

Dissolution:

Stage 1) Test 6 units (Result = % released at specified dissolution time point)

Pass if the following criteria are met:

1) All 6 results $\geq Q + 5$

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 $\leq Q - 15$

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 $\leq Q - 25$