

VALIDATION REPORT

Content uniformity and Dissolution Acceptance Limits (CuDAL) Version 2



Content uniformity and Dissolution Acceptance Limits (CuDAL) Version 2 is a set of SASTM programs used to evaluate data against the current USP 29 content uniformity and dissolution tests. Validation of these programs has been successfully completed.

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VALIDATION SUMMARY

Validation of CuDAL (Version 2) is complete. Any problems/issues that identified during the validation process were resolved. Problems/issues that required changes to the navigation/input or calculations were retested using the appropriate test data. After making changes to the navigation/input or calculations, the programs were sent to the validation leads to insure that the program loaded properly. The following sections of this report contain the test objectives/requirements and summarize the problems/issues found during the validation process. All issues were satisfactorily resolved and the validation successfully completed.

Test Objectives/Requirements

Validation testing ensured that the system met the needs of the business users as listed below:

- Successfully open the CuDAL.sas.
- Successfully edit CuDAL to provide location of other required files.
- Successfully submit CuDAL.sas and obtain initial graphic user interface (GUI) window.
- Successfully exit SAS from initial window.
- Successfully enter the application.
- Provide a window that lists tests (content uniformity and dissolution) and sampling plan choices (sampling plan 1 or 2).
- Successfully select any of the four test/sampling plan combinations.
- Provide appropriate window for each selected test/sampling plan.
- Successfully input required numeric analysis information for each test/sampling plan.
 - Content Uniformity - Sampling Plan 1
 - Sample Size
 - Target
 - Lower Bound
 - Confidence Level
 - Content Uniformity - Sampling Plan 2
 - Number of Locations
 - Number per Location
 - Target
 - Lower Bound
 - Confidence Level
 - Dissolution - Sampling Plan 1
 - Q
 - Sample Size
 - Lower Bound (Numeric)
 - Confidence Level (Numeric)

- Dissolution - Sampling Plan 2
 - Q
 - Number of Locations
 - Number per Location
 - Target
 - Lower Bound
 - Confidence Level
 - Increments for Output Table Between and Within Standard Deviations.
- Generate error window if numeric data is not within allowable ranges.
- Successfully select desired analyses for each selected test/sampling plan.
 - Print Acceptance Limit Table
 - Evaluation of Probability to Pass Acceptance Limit Table
 - Find Lower Bound for specific sample results.
- Print the following acceptance limit tables:
 - Sampling Plan 1 -list means and corresponding CV limits.
 - Sampling Plan 2 - provide a range (lower and upper means) for various combinations of within and between location standard deviations.
- If an evaluation of probability to pass the acceptance limit table is selected, the program successfully provides a window for the user to enter the following required numeric information.
 - Range of Population means and CV's for Sampling Plan 1
 - Range of Population means, Between Location Standard Deviations, and Within Location Standard Deviations for Sampling Plan 2
- If the user requests finding a lower bound for a specific sample result, the program successfully provides a window for the user to enter the following required information.
 - Sample Mean and CV for Sampling Plan 1
 - Sample Mean, Between Location Standard Deviation, and Within Location Standard Deviation for Sampling Plan 2
- If an evaluation of probability to pass the acceptance limit table is selected, the program outputs a table listing the population values that were requested by the user and the probability that sample results will pass the table.
- If the user requests finding a lower bound for a specific sample result, the program successfully outputs the sample values that were given by the user and the lower bound probability.
- The program successfully allows the user to navigate the program.
 - After analysis of a test/sampling plan returns to the initial screen for that chosen combination.
 - Clicking on a Cancel button returns the user to a "higher level" window.
 - The user successfully returns to the test/sampling plan request window or initial opening window by clicking on a cancel button.

Validation Steps

The validation was performed in the following five steps (See original protocol):

1) Load and run the program (See signed Form 1's)

Comments: All team members were able to load and run the program after the navigation program was revised to include the CuDAL logo (See amendment 2). Two members used version 9 of SAS. The other members of the validation team used version 8. Only the validation leads tested loading of the program after subsequent changes to the program since these changes did not affect the navigation or input.

2) Navigate and Test for input errors in the primary windows (See signed Form 2, test data).

3) Verify the mathematical calculations for the lower bounds (See signed Form 3).

4) Verify program strategy and SAS code (See signed Form 4).

5) Perform calculations of test data using an independent program (See signed Form 5).

Problems/Issues Discovered During Validation

Table 1 lists the problems found and corrected during validation. The table indicates where the problem was identified and what parts of the validation were affected by the problem. There were five Problem Request Report forms (See request forms) and five amendments (See amendments) generated during the course of the validation. As can be seen in Table 1, there was a total of seven problems to correct. Three problems required revision of the navigation/input portion of the program and three problems required changes to the calculations. All problems were corrected and verified using corrected test data or by an independent program. There was one incidence of disagreement between the test data expected results and found results which occurred in the independent code testing. The CuDAL result for an acceptable CV in one case for sampling plan 1 was 4.88. The independent code calculation performed using SPLUS was 4.87. An investigation indicated that the difference in results was due to how the two programs round the number 4.875. SAS rounds up whereas SPLUS (which was used to provide an independent check) rounds down. This disagreement is considered acceptable by the validation team.

As stated in the validation protocol, the dissolution program was not changed from version 1 to version 2 of CuDAL. Therefore, the only test performed was to generate a table using sampling plan 1 and sampling plan 2 using both Version 1 and Version 2 and comparing the output. For both sampling plans, the two sets of output matched.

Table 1
Problems Found During Validation

Problem Source	Problem	Affected			Amendment # Addressing Problem
		Protocol	SAS Program Navigation/Input	SAS Program Calculations	
Protocol	Typographical errors in equations.	X			1
Navigation/Input	CuDAL logo did not appear in opening window	X	X		2
	Sample mean input for content uniformity and dissolution were compared to both content uniformity and dissolution acceptable ranges instead of just their respective ranges.	X	X		2
	Test Data Misprint for Dissolution when sample mean is equal to Q	X			4
Calculations	Program calculations based on incorrect interpretation of USP test for individual results at stage 2. Should be as % of M instead of % of Target	X		X	3
	Error in one line of SAS code that calculates probability at stage 2 of uniformity of all 30 results lying between 75-125% of M	X		X	5
	Misplaced Assignment of the Macro variable "TARGET"	X		X	5

Content Uniformity and Dissolution Acceptance Limit Program

VALIDATION PROTOCOL **Version 2.0**

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PROTOCOL

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- F PROGRAM DESCRIPTION
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FORMS

- 1 LOAD AND RUN PROGRAM
- 2 PRIMARY WINDOW NAVIGATION
& INPUT ERROR CHECKS
- 3 MATHEMATICAL CALCULATION VERIFICATION
- 4 PROGRAM STRATEGY & SAS CODE VERIFICATION
- 5 TEST DATA AGREEMENT
- 6 PROBLEM/REQUEST REPORT

PROTOCOL

PURPOSE:

Version 2 of a program that generates content uniformity and dissolution acceptance limits (CuDAL) will be conducted to verify its functionality and reliability in generating acceptance limit tables based on user input.

OVERVIEW:

As part of the International Conference on Harmonization (ICH) effort, the USP has revised general chapter <905>, Uniformity of Dosage Units. The revised, harmonized general chapter Uniformity of Dosage Units <905> printed in *United States Pharmacopeia* 28-NF 23 (1) will take affect in 2007. The final revised version is a result of many discussions as well as several evaluations and recommendations by the PhRMA CMC Statistics Expert Team (2, 3, 4). Bergum (5) published a method for constructing acceptance limits that relates the acceptance criteria directly to multiple stage tests such as the USP content uniformity and dissolution tests. Bergum and Utter (6, 7) discussed several statistical techniques for evaluating content uniformity. Bergum (8) wrote a SASTM program that implements his method. The program performs the calculations and generates acceptance limit tables. Since the USP test for content uniformity has been revised, new mathematical calculations for content uniformity and a revised SASTM program were developed to generate acceptance limit tables. No changes were needed for dissolution.

The acceptance limits are defined to provide, with a stated confidence level $(1 - \alpha)100\%$, that there is at least a stated probability (P) that a sample taken from a batch would pass the content uniformity test. For example, one can make the statement that, with 95% confidence, there is at least a 95% probability that future samples from the batch will pass the USP content uniformity test. For the revised USP test, these tables change with the confidence level $(1 - \alpha)$, the probability bound (P), the sample size (n) and the target content per dosage unit. Confidence levels as well as values for P are typically 50%, 90%, or 95%. A PDA Technical Report (9) suggests the use of a 90% confidence level to provide 95% coverage. A 50% confidence level can be considered a “best estimate” of the coverage.

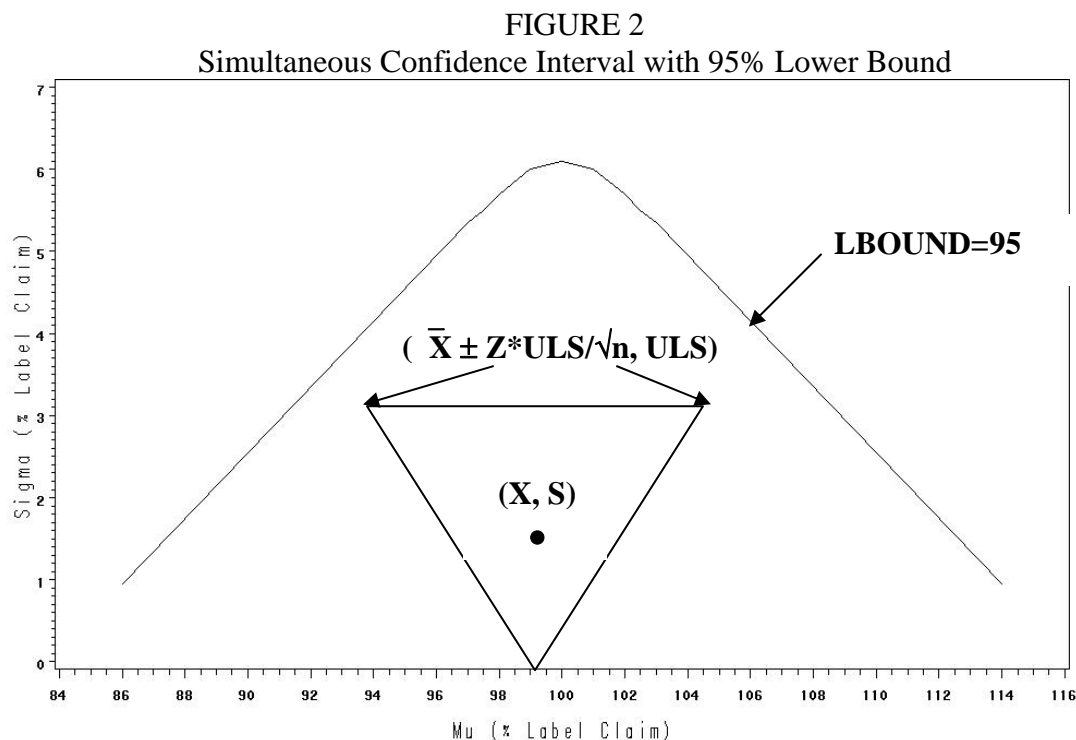
Constructing Acceptance Limits

Assume that the content uniformity test results follow a normal distribution with mean μ and standard deviation σ . Sigma (σ) is the standard deviation of a single observation. For a given value of μ and a given value of σ , a lower bound (LBOUND) can be determined (See Appendix E for detailed calculations).

The LBOUND can be used to develop acceptance limits. This is done by first constructing a simultaneous confidence interval for μ and σ from the data. If a 90% confidence interval is constructed for μ and σ and the entire interval is below the 95% LBOUND, then with 90% confidence, at least 95% of the samples tested would pass the USP test.

Construction of the confidence intervals depends on the sampling plan used to collect the samples. There are two sampling plans that are generally used when testing blends or final product. In the first plan (Sampling Plan 1), a single test result is obtained from each location sampled. For example, in a blending step, a single test result would be obtained from each of a number of different locations within the blender. In a drum, a single test result might be obtained from the different locations within the drum or from each of a number of different drums. For final tablets, a single tablet may be tested from various time points throughout the tableting run. In the second plan (Sampling Plan 2), more than one test result is obtained from each of the sampled locations. For example, during the tableting operation, if a cup is placed under the tablet press at specific time points during the tableting run, several of the tablets from each cup sample would be tested for content uniformity. Sampling Plan 2 allows for estimation of between location and within location variability.

For Sampling Plan 1, the sample mean and sample standard deviation estimate the population parameters μ and σ . A simultaneous confidence interval for μ and σ is given in Lindgren (10). The interval and the 95% LBOUND are displayed in Figure 2 where ULS is the upper confidence limit for σ and Z is a standard normal critical value.



Once the confidence interval is constructed, it must fall completely below the specified LBOUND. An acceptance limit table can be generated by finding the largest sample standard deviation for a fixed sample mean such that the resulting confidence interval remains below the pre-specified LBOUND. Note that the only two points to evaluate on the triangle are the two points with the maximum value of sigma.

CuDAL is a set of programs written by James Bergum in SAS™ that can be used to evaluate content uniformity and dissolution data against the current USP XXIII tests. The program will generate an acceptance limit table for content uniformity and/or dissolution that can be applied when using two specific 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 a specific sample result. 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 value of P and C are provided by the user.

DESCRIPTION OF SYSTEM SOFTWARE:

CuDAL was written using SAS™. The program consists of seven files. CuDAL.SAS is the file that contains the file location and is used to launch the program. There are four files that perform the calculations and generate SAS output (CuDAL.SAS, CUSP1.SAS, CUSP2.SAS, DISP1.SAS, and DISP2.SAS). Each file is a Macro written in SAS™. A hardcopy of these programs is given in Appendix A. There are two files (cudal.sas7bcat and Files.sas.org) that provide the graphical user interface (GUI) for user input and navigation of the program. The user interface was written by Saritha Aleti. The windows displayed for user input during the execution of the program are listed in Appendix B. If an input error is made by the user, an error window is displayed. The software was designed to run on any IBM or compatible PC that has SAS™ 8.02 or later.

DESCRIPTION OF SYSTEM HARDWARE:

CuDAL was written in SAS™ Version 8.02 to run on any IBM or compatible PC that has SAS 8.02 or later on it. There are no additional hardware requirements. The PC's used in the validation of CuDAL will be documented in the validation report.

ASSUMPTIONS, EXCLUSIONS, AND OPERATIONAL LIMITATIONS:

The CuDAL program will operate using the appropriate PC hardware and software. There are no operational limits that have been identified at the time of this validation. Since SAS™ is an accepted vendor supplied software package, validation of the SAS™ program itself is not necessary.

The PC's used in the CuDAL validation are considered validated with respect to mice, keyboards, printers, monitors, and diskette drives.

TEST OBJECTIVES/REQUIREMENTS

This testing ensures that the system meets the needs of the business users as listed below:

- User can successfully open the CuDAL.sas.
- User can successfully edit CuDAL to provide location of other required files.
- User can successfully submit CuDAL.sas and obtain initial graphic user interface (GUI) window.
- User can successfully exit SAS from initial window.
- User can successfully enter the application.
- Program can provide a window that lists tests (content uniformity and dissolution) and sampling plan choices (sampling plan 1 or 2).
- User can successfully select any of the four test/sampling plan combinations.
- Program can provide appropriate window for each selected test/sampling plan.
- User can successfully input required numeric analysis information for each test/sampling plan.
 - Content Uniformity - Sampling Plan 1
 - Sample Size
 - Target
 - Lower Bound
 - Confidence Level
 - Content Uniformity - Sampling Plan 2
 - Number of Locations
 - Number per Location
 - Target
 - Lower Bound
 - Confidence Level
 - Dissolution - Sampling Plan 1
 - Q
 - Sample Size
 - Lower Bound (Numeric)
 - Confidence Level (Numeric)
 - Dissolution - Sampling Plan 2
 - Q
 - Number of Locations

- Number per Location
 - Target
 - Lower Bound
 - Confidence Level
 - Increments for Output Table Between and Within Standard Deviations.
- Program will generate error window if numeric data is not within allowable ranges.
- User can successfully select desired analyses for each selected test/sampling plan.
 - Print Acceptance Limit Table
 - Evaluation of Probability to Pass Acceptance Limit Table
 - Find Lower Bound for specific sample results.
- If a print of the acceptance limit table is selected, the program will output a table:
 - The Sampling Plan 1 table will list means and corresponding CV limits.
 - The Sampling Plan 2 table will provide a range (lower and upper means) for various combinations of within and between location standard deviations.
- If an evaluation of probability to pass the acceptance limit table is selected, the program will successfully provide a window for the user to enter the following required numeric information.
 - Range of Population means and CV's for Sampling Plan 1
 - Range of Population means, Between Location Standard Deviations, and Within Location Standard Deviations for Sampling Plan 2
- If the user requests finding a lower bound for a specific sample result, the program will successfully provide a window for the user to enter the following required information.
 - Sample Mean and CV for Sampling Plan 1
 - Sample Mean, Between Location Standard Deviation, and Within Location Standard Deviation for Sampling Plan 2
- If an evaluation of probability to pass the acceptance limit table is selected, the program will output a table listing the population values that were requested by the user and the probability that sample results will pass the table.
- If the user requests finding a lower bound for a specific sample result, the program will successfully output the sample values that were given by the user and the lower bound probability.
- The program will successfully allow the user to navigate the program.
 - After analysis of a test/sampling plan will return to the initial screen for that chosen combination.
 - Clicking on a Cancel button will return the user to a "higher level" window.
 - The user can successfully return to the test/sampling plan request window or initial opening window by clicking on a cancel button.

VALIDATION PLAN:

The validation team to perform validation of CuDAL consists of the following individuals:

Stan Alton, J&J Pharmaceutical R&D
Myron Diener, Sanofi-Aventis
Yijie Dong, Bristol-Myers Squibb
Brent Harrington, Wyeth Research
David LeBlond, Abbott
James Pazdan, Novartis Pharmaceuticals
Edith Senderak, Merck & Company, Inc.
Merlin Utter, Wyeth Pharmaceuticals
Rowland Yovonie, Hoffmann-La Roche Inc.

CV's from each member of the validation team will be included in the supporting documentation.

There are three validation sub-teams. Each sub-team will have a lead responsible for signing the validation protocol, validation summary report, and appropriate forms as described in the Validation Step section of the protocol.

1) Macro strategy, SAS™ code, and Mathematical calculations:

Yijie Dong (Lead)
Stan Alton
James Pazdan
Edith Senderak
Rowland Yovonie

2) Navigation & Window Input Error Checking:

Myron Diener (Lead)

3) Test Data Evaluation and Independent Calculations-

Merlin Utter (Lead)
Brent Harrington
David LeBlond

The validation steps are described below:

VALIDATION STEPS

1) LOAD AND RUN PROGRAM

Each member of the validation team will:

1. Copy the program files (CuDAL.SAS, CUSP1.SAS, CUSP2.SAS, DISP1.SAS, and DISP2.SAS, cudal.sas7bcat, and Files.sas.org) to their computer
2. Modify the file CuDAL.SAS to indicate location of the files on their PC
3. Submit the program CuDAL.SAS
4. Click on “Enter the Application” on the opening window.
5. Select one of the test/sampling plan combinations.
6. Select Y for all three analyses (Print Table, Evaluate Table, and obtain Lower bound for a specific sample result)
7. Use the default values for all numeric inputs.
8. Compare the output to the appropriate expected output found in Appendix C.
9. Fill out Form 1 to verify that the program loaded properly and the appropriate output was generated.

2) NAVIGATION & TEST FOR INPUT ERRORS IN PRIMARY WINDOWS

The Navigation & Error Checking Sub-team will insure that the program allows the user to navigate through the GUI windows and that the program displays specific error checks. Test data are contained in Appendix D listing the window, requested input, test input, expected response, found response, and a column to record agreement between expected and found response. The Error Checking sub-team will indicate a Y or N in this column after each test indicating whether or not an error window was displayed. Once all error test data checks are complete, Form 2 will be filled out indicating whether or not all error checks passed.

3) VERIFY MATHEMATICAL CALCULATIONS FOR LOWER BOUND

Appendix E contains the mathematical calculations used to calculate the lower bound for each test. Since changes to the dissolution programs only involve user input and not the calculations, only the content uniformity calculations require verification. These calculations will be reviewed by the Macro strategy, SAS code, and Mathematical calculation sub-team for appropriateness & accuracy. Form 3 will be filled out indicating that these calculations were reviewed and are considered correct.

4) **VERIFY PROGRAM STRATEGY AND SAS CODE**

The program will be reviewed by the Macro strategy, SAS™ code, and Mathematical calculation sub team to verify that the strategy is correct, the code implements the strategy correctly, and that the mathematical calculations are implemented correctly. A complete description of the SAS™ programs is given in Appendix F. Since the only changes to the dissolution programs involved user input and not the calculations, only the content uniformity calculations require verification. Form 4 will be filled out to indicate that each macro has been reviewed for strategy, correct code, and mathematical lower bound implementation.

5) **RUN TEST DATA SETS:**

The test data sets are given in Appendix G. The validation team will compare two sets of acceptance limit table results. For content uniformity, the first set of results will be obtained by running the CuDAL program using the specified input values given in the test data set. The second set of results will be obtained by performing an independent calculation of the acceptance limit table result. This calculation will be performed using a software package other than SAS. The validation member performing these calculations will provide software and program details used to perform the calculations. The validation team member performing this part of the validation will fill in the final three columns in the test data table indicating the CuDAL program result, independent calculation result, and whether or not both calculations agree with one another. Results should agree after rounding to the number of digits given in the CuDAL result. For dissolution, independent calculations are not required since the calculations have not changed since version 1. However, Appendix G contains two dissolution tables (sampling plan1 & 2) generated using version 1. These tables will be compared to the dissolution tables generated by version 2.

CRITERIA FOR ACCEPTANCE:

Forms 1- 5 are all signed indicating that the program loaded and ran successfully, input errors return error windows, the mathematical calculations for the lower bound is correct, the strategy used is appropriate, the SAS™ code is correct, and the test data expected result agreed with both the CuDAL output from the validation members own run and the result from the independent calculation.

It will be the responsibility of the validation team leads to determine what impact any problems encountered, either singularly or in total, will have on this validation. The decision to continue or terminate this validation will be made by the validation team leads.

For ultimate acceptance, the program should perform as described without any failure that would compromise the user's confidence in the reliability of this program.

ERROR RESOLUTION:

Errors (discrepancies in results versus expected performance) detected during testing will be recorded on a Problem/Request Report form. A request for error resolution will be transmitted to the programmer (James Bergum). The validation team leads will evaluate and approve/accept all error resolutions received from the programmer.

DOCUMENTATION:

Once validation is done, the following documentation will be placed on a Recordable CD for distribution:

- 1) Version 2 Programs
- 2) Version 2 Validation protocol
- 3) Version 2 Validation report
- 4) Version 1 Validation report

Any additional supporting documentation will be kept by James Bergum.

RESPONSIBILITIES AND AUTHORITY:

Validation protocol preparation: James Bergum

Approval of validation protocol: Validation Sub-Team Leads

Execution of testing procedures: Validation Sub-Team Leads

Evaluation of validation study results: Validation Sub-Team Leads

Preparation of validation study report: James Bergum

Approval of validation study report: Validation Sub-Team Leads

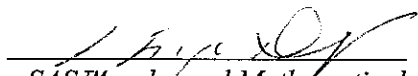
PROTOCOL CHANGES:

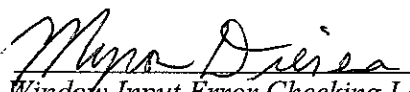
Any changes or revisions of the protocol, and reasons for them, will be documented, dated, and signed by the validation team and will be retained as amendments to the protocol.


REFERENCES

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2. Content Uniformity—Evaluation of the USP Pharmacopeial Preview Pharmacopeial Forum, Vol. 24, No. 5 Sept.-Oct. 1998: 7029-7044
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10. Lindgren, B.W. *Statistical Theory* New York: Macmillan (1968).
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PROTOCOL APPROVAL

Name:  Date: 5/10/07
Macro strategy, SASTM code, and Mathematical calculations Lead

Name  Date: 5/10/07
Navigation & Window Input Error Checking Lead

Name  Date: 05/10/2007
Test Data Evaluation and Independent Calculations Lead

APPENDIX A PROGRAMS

CHANGES FROM VERSION 1

CuDAL.SAS

```
1. ***** LIBRARY FOR THE APPLICATION*****;
2. /* deleting the macro variables */
3. data vars;
      i. set sashelp.vmacro;
4. run;
5. data _null_;
      i. set vars;
      ii. if scope='GLOBAL' and name ^= 'SYSODSPATH' then
      iii. call execute('%syndel '||trim(left(name))|| ';' );
6. run;

7. libname cudal 'F:\My Documents\My SAS files\V8\CuDAL\V2';
8. options symbolgen mprint mlogic sasautos=('F:\My Documents\My SAS
   files\V8\CuDAL\V2');

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

CUSP1.SAS

```
1. %MACRO CUSP1(A1CUSP1=,
2. A2CUSP1=,
3. A3CUSP1=);
4. %LET D=0.1;

5. data _null_;
6. set mcusp1;
7. CALL SYMPUT( "NUMBER", PUT(LNUMBER, 4.0));
8. CALL SYMPUT( "T", PUT(LT, 5.1));
9. CALL SYMPUT( "LBOUND", PUT(LLBOUND, 4.1));
10. CALL SYMPUT( "CILEVEL", PUT(LCILEVEL, 4.1));
11. run;

12. %IF %UPCASE(&A2CUSP1)=Y %THEN %DO;
13. data _null_;
14. set ev1;
15. CALL SYMPUT( "ULOW", PUT(LULOW, 4.0));
16. CALL SYMPUT( "UHIGH", PUT(LUHIGH, 4.0));
17. CALL SYMPUT( "UINCRE", PUT(LUINCRE, 4.0));
18. CALL SYMPUT( "UDIV", PUT(LUDIV, 4.0));
19. CALL SYMPUT( "CVLOW", PUT(LCVLOW, 4.0));
20. CALL SYMPUT( "CVHIGH", PUT(LCVHIGH, 4.0));
21. CALL SYMPUT( "CVINCRE", PUT(LCVINCRE, 4.0));
22. CALL SYMPUT( "CVDIV", PUT(LCVDIV, 4.0));
23. RUN;
24. %END;
25. %ELSE %IF %UPCASE(&A2CUSP1)=N %THEN %DO;
26. data _null_;
27. CALL SYMPUT( "ULOW", PUT(950, 4.0));
28. CALL SYMPUT( "UHIGH", PUT(1000, 4.0));
```

```

29. CALL SYMPUT( "UINCRE", PUT( 50, 4.0 ) );
30. CALL SYMPUT( "UDIV", PUT( 10, 4.0 ) );
31. CALL SYMPUT( "CVLOW", PUT( 10, 4.0 ) );
32. CALL SYMPUT( "CVHIGH", PUT( 40, 4.0 ) );
33. CALL SYMPUT( "CVINCRE", PUT( 30, 4.0 ) );
34. CALL SYMPUT( "CVDIV", PUT( 10, 4.0 ) );
35. RUN;
36. %END;

37. %IF %UPCASE(&A3CUSP1)=Y %THEN %DO;
38. data _null_;
39. set smpl;
40. CALL SYMPUT( "MEAN", PUT( LMEAN, 6.3 ) );
41. CALL SYMPUT( "CV", PUT( LCV, 6.3 ) );
42. CALL SYMPUT( "LCV", PUT( LCV, 6.3 ) );

43. run;
44. %END;
45. %IF %UPCASE(&A3CUSP1)=N %THEN %DO;
46. data _null_;
47. CALL SYMPUT( "MEAN", PUT( 100, 6.3 ) );
48. CALL SYMPUT( "CV", PUT( 4, 6.3 ) );
49. CALL SYMPUT( "LCV", PUT( 4, 6.3 ) );
50. run;
51. %END;

52. %macro clcalc;
53. mu=LLU;
54. n1=10;
55. n2=30;
56. k1=2.4;
57. k2=2.0;
58. L1=15;
59. L2=25;
60. if TARGET LE 101.5 then E =101.5;
61. else E = TARGET;

62. z1=(E-mu)*sqrt(n1)/sigma;
63. z2=( 98.5-mu)*sqrt(n1)/sigma;
64. chi1=probchi( (n1-1)*L1**2/(k1*sigma)**2, n1-1 );
65. int1=(probnorm(z1)-probnorm(z2))*chi1;
66. t=1;
67. h=0.05;
68. int2=0;
69. do x=E to (E+15-h) by h;
70. x1=(x-mu)*sqrt(n1)/sigma;
71. x2=(x+h-mu)*sqrt(n1)/sigma;
72. chi2=(n1-1)*(E+15-x-h/2)**2/(k1*sigma)**2;
73. int2=int2+(probnorm(x2)-probnorm(x1))*probchi(chi2, n1-1);
74. end;

75. int3=0;
76. do x=( 98.5-15) to ( 98.5-h) by h;
77. x1=(x-mu)*sqrt(n1)/sigma;
78. x2=(x+h-mu)*sqrt(n1)/sigma;
79. chi3=(n1-1)*( 15-98.5+x+h/2)**2/(k1*sigma)**2;
80. int3=int3+(probnorm(x2)-probnorm(x1))*probchi(chi3, n1-1);

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81.      end;

82.      P1=int1+int2+int3;

83.      zz1=(E-mu)*sqrt(n2)/sigma;
84.      zz2=(98.5-mu)*sqrt(n2)/sigma;
85.      cchi1=probchi((n2-1)*L1**2/(k2*sigma)**2, n2-1);
86.      iint1=(probnorm(zz1)-probnorm(zz2))*cchi1;
87.      iint2=0;
88.      do xx=E to (E+15-h) by h;
89.          xx1=(xx-mu)*sqrt(n2)/sigma;
90.          xx2=(xx+h-mu)*sqrt(n2)/sigma;
91.          cchi2=(n2-1)*(E+15-xx-h/2)**2/(k2*sigma)**2;
92.          iint2=iint2+(probnorm(xx2)-probnorm(xx1))*probchi(cchi2,
n2-1);
93.      end;

94.      iint3=0;
95.      do xx=(98.5-15) to (98.5-h) by h;
96.          xx1=(xx-mu)*sqrt(n2)/sigma;
97.          xx2=(xx+h-mu)*sqrt(n2)/sigma;
98.          cchi3=(n2-1)*(15-98.5+xx+h/2)**2/(k2*sigma)**2;
99.          iint3=iint3+(probnorm(xx2)-probnorm(xx1))*probchi(cchi3,
n2-1);
100.     end;

101.     P2a=iint1+iint2+iint3;

102.     zzz1=(123.5-mu)/sigma;
103.     if TARGET LE 101.5 then zzz2=(101.5-25-mu)/sigma;
104.     else zzz2 = (TARGET-25-mu)/sigma;

105.     P2b=(probnorm(zzz2)-probnorm(zzz1))*30;

106.     P2=max(0, P2a+P2b-1);

107.     overlbd=max(P1, P2);

108.     mu=ULU;
109.     n1=10;
110.     n2=30;
111.     k1=2.4;
112.     k2=2.0;
113.     L1=15;
114.     L2=25;

115.     z1=(E-mu)*sqrt(n1)/sigma;
116.     z2=(98.5-mu)*sqrt(n1)/sigma;
117.     chil=probchi((n1-1)*L1**2/(k1*sigma)**2, n1-1);
118.     int1=(probnorm(z1)-probnorm(z2))*chil;
119.     t=1;
120.     h=0.05;
121.     int2=0;
122.     do x=E to (E+15-h) by h;
123.         x1=(x-mu)*sqrt(n1)/sigma;

```

```

124.     x2=(x+h-mu)*sqrt(n1)/sigma;
125.     chi2=(n1-1)*(E+15-x-h/2)**2/(k1*sigma)**2;
126.     int2=int2+(probnorm(x2)-probnorm(x1))*probchi(chi2, n1-1);
127.     end;

128.     int3=0;
129.     do x=(98.5-15) to (98.5-h) by h;
130.     x1=(x-mu)*sqrt(n1)/sigma;
131.     x2=(x+h-mu)*sqrt(n1)/sigma;
132.     chi3=(n1-1)*(15-98.5+x+h/2)**2/(k1*sigma)**2;
133.     int3=int3+(probnorm(x2)-probnorm(x1))*probchi(chi3, n1-1);
134.     end;

135.     P1=int1+int2+int3;

136.     zz1=(E-mu)*sqrt(n2)/sigma;
137.     zz2=(98.5-mu)*sqrt(n2)/sigma;
138.     cchi1=probchi((n2-1)*L1**2/(k2*sigma)**2, n2-1);
139.     iint1=(probnorm(zz1)-probnorm(zz2))*cchi1;
140.     iint2=0;
141.     do xx=E to (E+15-h) by h;
142.     xx1=(xx-mu)*sqrt(n2)/sigma;
143.     xx2=(xx+h-mu)*sqrt(n2)/sigma;
144.     cchi2=(n2-1)*(E+15-xx-h/2)**2/(k2*sigma)**2;
145.     iint2=iint2+(probnorm(xx2)-probnorm(xx1))*probchi(cchi2,
n2-1);
146.     end;

147.     iint3=0;
148.     do xx=(98.5-15) to (98.5-h) by h;
149.     xx1=(xx-mu)*sqrt(n2)/sigma;
150.     xx2=(xx+h-mu)*sqrt(n2)/sigma;
151.     cchi3=(n2-1)*(15-98.5+xx+h/2)**2/(k2*sigma)**2;
152.     iint3=iint3+(probnorm(xx2)-probnorm(xx1))*probchi(cchi3,
n2-1);
153.     end;

154.     P2a=iint1+iint2+iint3;

155.     zzz1=(123.5-mu)/sigma;
156.     if TARGET LE 101.5 then zzz2=(101.5-25-mu)/sigma;
157.     else zzz2 = (TARGET-25-mu)/sigma;

158.     P2b=(probnorm(zzz2)-probnorm(zzz1))**30;

159.     P2=max(0, P2a+P2b-1);

160.     overubd=max(P1, P2);

161.     OVERBD = MIN(OVERLBD, OVERUBD);
162.     %mend clcalc;

163.     %MACRO CALCUSP1;
164.     DATA TAB;
165.     LABEL OVERBD = 'OVERALL LOWER BOUND'
-     MEAN = 'SAMPLE MEAN(%CLAIM)';

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```

166.      D=&D;
167.      Z = PROBIT((1 + SQRT(&CILEVEL / 100)) / 2);
168.      N = &NUMBER;
169.      TARGET = &T;
170.      CHI = CINV(1 - SQRT(&CILEVEL / 100),N - 1);
171.      SDOLD = 0;
172.      STARTSD = 0.01;
173.      DO MEAN = 85.1 TO 114.9 BY D;
174.      BEGIN = STARTSD;
175.      DO SAMPSD = BEGIN TO 7.8 BY 0.001;
176.      SIGMA = SQRT((N - 1) * SAMPSD * SAMPSD / CHI);
177.      LLU = MEAN - Z * SIGMA / SQRT(N);
178.      ULU = MEAN + Z * SIGMA / SQRT(N);
179.      %c1calc
180.      IF OVERBD < &LBOUND/100 AND SAMPSD <= 0.0101 THEN DO;
181.      CV = 0; OUTPUT; SAMPSD = 20.0; GOTO NEXTT; END;
182.      IF OVERBD < &LBOUND/100 THEN DO;
183.      SAMPSD = SAMPSD - 0.001;
184.      IF SAMPSD < SDOLD THEN DO;
-      STARTM = MEAN;
-      GOTO UPPER;
        i. END;
185.      SDOLD = SAMPSD;
186.      STARTSD = SAMPSD;
187.      CV = 100 * SAMPSD / MEAN;
-      OUTPUT;
-      SAMPSD = 20.0;
-      END;
188.      NEXTT:
189.      END;
190.      END;
191.      GOTO FINISH;
192.      UPPER:
        i. STARTSD = 0.01;

193.      DO MEAN = 114.9 TO STARTM BY -D;
194.      DO SAMPSD = STARTSD TO 7.8 BY 0.001;
195.      SIGMA = SQRT((N - 1) * SAMPSD * SAMPSD / CHI);
196.      LLU = MEAN - Z * SIGMA / SQRT(N);
197.      ULU = MEAN + Z * SIGMA / SQRT(N);
198.      %c1calc
199.      IF OVERBD < &LBOUND/100 AND SAMPSD <= 0.0101 THEN DO;
200.      CV = 0; OUTPUT; SAMPSD = 20.0; GOTO NEXTB; END;
201.      IF OVERBD < &LBOUND/100 THEN DO;
202.      SAMPSD = SAMPSD - 0.001;
203.      STARTSD = SAMPSD;
204.      CV = 100 * SAMPSD / MEAN;
-      OUTPUT;
-      SAMPSD = 20.0;
-      END;
205.      NEXTB:
206.      END;
207.      END;
208.      FINISH:
209.      KEEP CV MEAN;
210.      PROC SORT DATA=TAB; BY MEAN;
211.      DATA

```

```

212.     ONE(RENAME = (MEAN = X1 CV = CV1))
213.     TWO(RENAME = (MEAN = X2 CV = CV2))
214.     THREE(RENAME = (MEAN = X3 CV = CV3))
215.     FOUR(RENAME = (MEAN = X4 CV = CV4))
216.     FIVE(RENAME = (MEAN = X5 CV = CV5))
217.     SIX(RENAME = (MEAN = X6 CV = CV6));
218.     SET TAB;
219.     IF MEAN <= 90.05 THEN OUTPUT ONE;
220.     IF 90.05 < MEAN <= 95.05 THEN OUTPUT TWO;
221.     IF 95.05 < MEAN <= 100.05 THEN OUTPUT THREE;
222.     IF 100.05 < MEAN <= 105.05 THEN OUTPUT FOUR;
223.     IF 105.05 < MEAN <= 110.05 THEN OUTPUT FIVE;
224.     IF 110.05 < MEAN <= 115.0 THEN OUTPUT SIX;
225.     DATA SEVEN;
226.     MERGE ONE TWO THREE FOUR FIVE SIX;
227.     RUN;
228.     %MEND CALCUSP1;

229.     %MACRO PRTCUSP1;
230.     OPTIONS MISSING = ' ' NODATE NONUMBER;
231.     OPTIONS LS=132;
232.     PROC PRINT DATA=SEVEN SPLIT = '*';
233.     FORMAT CV1 CV2 CV3 CV4 CV5 CV6 5.2;
234.     LABEL
-     X1 = ' MEAN*(% CLAIM) '
-     X2 = ' MEAN*(% CLAIM) '
-     X3 = ' MEAN*(% CLAIM) '
-     X4 = ' MEAN*(% CLAIM) '
-     X5 = ' MEAN*(% CLAIM) '
-     X6 = ' MEAN*(% CLAIM) '
-     CV1 = 'CV*(%) '
-     CV2 = 'CV*(%) '
-     CV3 = 'CV*(%) '
-     CV4 = 'CV*(%) '
-     CV5 = 'CV*(%) '
-     CV6 = 'CV*(%) ';
235.     VAR CV1 X2 CV2 X3 CV3 X4 CV4 X5 CV5 X6 CV6;
236.     ID X1;
237.     TITLE1 "ACCEPTANCE LIMITS FOR CONTENT UNIFORMITY(N=&NUMBER,
TARGET = &T)";
238.     TITLE2 "SAMPLING PLAN 1";
239.     TITLE3 "(MEETING LIMITS GUARANTEES, WITH &CILEVEL.%
ASSURANCE, THAT AT LEAST";
240.     TITLE4 "&LBOUND.% OF SAMPLES TESTED FOR CONTENT UNIFORMITY
WILL PASS THE USP TEST)";
241.     %MEND PRTCUSP1;

242.     %MACRO EVCUSP1;

243.     DATA TAB;
244.     SET SEVEN;

245.     %MACRO DSCUSP1;
246.     %DO I = 1 %TO 6;
247.     DATA DATA&I;
-     SET TAB;
-     STD = X&I * CV&I / 100; RENAME X&I = X;

```

```

- KEEP X&I STD;
248. %END;

249. %MEND DSCUSP1;

250. %DSCUSP1

251. DATA ONE;
252. SET DATA1 DATA2 DATA3 DATA4 DATA5 DATA6;
253. N = &NUMBER;
254. RUN;

255. %MACRO SIGCUSP1;

256. %DO CV = &CVLOW %TO &CVHIGH %BY &CVINCRE;
257. %DO U = &ULOW %TO &UHIGH %BY &UINCRE;

- DATA SAVE;
    i. SET ONE END = LAST;
    ii. U = &U / &UDIV;
    iii. CV = &CV / &CVDIV;
    iv. SIGMA = U * CV / 100;
    v. PMEAN = PROBNORM((x - U) * SQRT(N) / SIGMA)
- PROBNORM((LAG(X) - U) * SQRT(N) / SIGMA);
    i. AVEHT = (STD + LAG(STD)) / 2;
    ii. PSTD = PROBCHI((N - 1) * AVEHT * AVEHT
        1. / (SIGMA * SIGMA), N - 1);
    iii. PT = PMEAN * PSTD ;
    iv. PTRAP + PT;
    v. IF LAST THEN OUTPUT;
- RUN;

258. PROC APPEND BASE = SAVEALL DATA = SAVE;

- %END;
259. %END;

260. %MEND SIGCUSP1;

261. %SIGCUSP1

262. OPTIONS NODATE NONUMBER;
263. PROC PRINT DATA = SAVEALL split = '*';
264. label ptrap = 'PROBABILITY*OF*PASSING';
265. VAR CV PTRAP;
266. ID U;
267. TITLE1 "ACCEPTANCE LIMIT TABLE FOR CONTENT
UNIFORMITY(N=&NUMBER)";
268. TITLE2 "SAMPLING PLAN 1";
269. TITLE3 'DETERMINE PROBABILITY OF PASSING ACCEPTANCE LIMIT
TABLE';
270. TITLE4 "CONFIDENCE LEVEL = &CILEVEL AND LOWER BOUND =
&LBOUND";
271. RUN;
272. %MEND EVCUSP1;

273. %MACRO SMPCUSP1;

```

```

274.    %let TARGET = &T;
275.    DATA TAB;
276.    LABEL OVERBD = 'OVERALL LOWER BOUND'
      - MEAN = 'SAMPLE MEAN(%CLAIM)';
277.    CILEVEL = &CILEVEL;
278.    Z = PROBIT((1 + SQRT(&CILEVEL / 100)) / 2);
279.    N = &NUMBER;
280.    CHI = CINV(1 - SQRT(&CILEVEL / 100), N - 1);
281.    MEAN = &MEAN;
282.    CV = &LCV;
283.    SAMPSD= &MEAN * CV/100;
284.    SIGMA = SQRT((N - 1) * SAMPSD * SAMPSD / CHI);
285.    LLU = MEAN - Z *SIGMA / SQRT(N);
286.    ULU = MEAN + Z * SIGMA / SQRT(N);
287.    %c1calc

288.    OPTIONS NODATE NONUMBER;
289.    PROC PRINT SPLIT = '*';
290.    LABEL SAMPSD = 'SAMPLE*STD DEV*(% CLAIM)'
      - MEAN = 'SAMPLE* MEAN*(% CLAIM)'
      - OVERBD = 'LOWER BOUND';
291.    ID MEAN;
292.    VAR SAMPSD CV OVERBD;
293.    TITLE1 "ACCEPTANCE LIMIT TABLE FOR CONTENT
      UNIFORMITY(N=&NUMBER)";
294.    TITLE2 "SAMPLING PLAN 1";
295.    TITLE3 'DETERMINE PROBABILITY OF FUTURE SAMPLES PASSING THE
      USP TEST';
296.    TITLE4 "WITH &CILEVEL ASSURANCE FOR GIVEN SAMPLE MEAN AND
      CV";
297.    run;
298.    %MEND SMPCUSP1;

299.    %MACRO ANACUSP1;
300.    %IF %UPCASE(&A1CUSP1)=Y OR %UPCASE(&A2CUSP1)=Y %THEN %DO;
301.    %CALCUSP1;
302.    %END;
303.    %IF %UPCASE(&A1CUSP1)=Y %THEN %DO;
304.    %PRTCUSP1;
305.    %END;
306.    %IF %UPCASE(&A2CUSP1)=Y %THEN %DO;
307.    %EVCUSP1;
308.    PROC DATASETS LIBRARY = WORK;
309.    DELETE SAVEALL;
310.    quit;
311.    %END;
312.    %IF %UPCASE(&A3CUSP1)=Y %THEN %DO;
313.    %SMPCUSP1;
314.    %END;
315.    %MEND ANACUSP1;

316.    %ANACUSP1

317.    RUN;
318.    %MEND CUSP1;
319.    %CUSP1

```

CUSP2.SAS

```
1. %MACRO CUSP2(A1CUSP2=,
2. A2CUSP2=,
3. A3CUSP2=);
4. %LET D1=0.10;

5. OPTIONS NODATE NONUMBER;

6. data _null_;
7. set mcusp2;
8. CALL SYMPUT("LOC",PUT(LLOC,4.0));
9. CALL SYMPUT("NUM",PUT(LNUM,4.0));
10. CALL SYMPUT("T",PUT(LT,5.1));
11. CALL SYMPUT("LBOUND",PUT(LLBOUND,4.1));
12. CALL SYMPUT("CILEVEL",PUT(LCILEVEL,4.1));
13. run;

14. %IF %UPCASE(&A2CUSP2)=Y %THEN %DO;
15. data _null_;
16. set ev2;
17. CALL SYMPUT("ULOW",PUT(LULOW,4.0));
18. CALL SYMPUT("UHIGH",PUT(LUHIGH,4.0));
19. CALL SYMPUT("UINCRE",PUT(LUINCRE,4.0));
20. CALL SYMPUT("UDIV",PUT(LUDIV,4.0));
21. CALL SYMPUT("SELOW",PUT(LSELOW,4.0));
22. CALL SYMPUT("SEHIGH",PUT(LSEHIGH,4.0));
23. CALL SYMPUT("SEINCRE",PUT(LSEINCRE,4.0));
24. CALL SYMPUT("SEDIV",PUT(LSEDIV,4.0));
25. CALL SYMPUT("SMLOW",PUT(LSMLOW,4.0));
26. CALL SYMPUT("SMHIGH",PUT(LSMHIGH,4.0));
27. CALL SYMPUT("SMINCRE",PUT(LSMINCRE,4.0));
28. CALL SYMPUT("SMDIV",PUT(LSMDIV,4.0));
29. RUN;
30. %END;
31. %ELSE %IF %UPCASE(&A2CUSP2)=N %THEN %DO;
32. data _null_;
33. CALL SYMPUT("ULOW",PUT(950,4.0));
34. CALL SYMPUT("UHIGH",PUT(1000,4.0));
35. CALL SYMPUT("UINCRE",PUT(50,4.0));
36. CALL SYMPUT("UDIV",PUT(10,4.0));
37. CALL SYMPUT("SELOW",PUT(22,4.0));
38. CALL SYMPUT("SEHIGH",PUT(22,4.0));
39. CALL SYMPUT("SEINCRE",PUT(10,4.0));
40. CALL SYMPUT("SEDIV",PUT(10,4.0));
41. CALL SYMPUT("SMLOW",PUT(22,4.0));
42. CALL SYMPUT("SMHIGH",PUT(22,4.0));
43. CALL SYMPUT("SMINCRE",PUT(10,4.0));
44. CALL SYMPUT("SMDIV",PUT(10,4.0));
45. RUN;
46. %END;

47. %IF %UPCASE(&A3CUSP2)=Y %THEN %DO;
48. data _null_;
```

```

49.      set smp2;
50.      CALL SYMPUT( "MEAN", PUT(LMEAN, 6.3) );
51.      CALL SYMPUT( "SE", PUT(LSE, 6.3) );
52.      CALL SYMPUT( "SM", PUT(LSM, 6.3) );
53.      run;
54.      %END;
55.      %ELSE %IF %UPCASE(&A3CUSP2)=N %THEN %DO;
56.      data _null_;
57.      CALL SYMPUT( "MEAN", PUT(100, 6.3) );
58.      CALL SYMPUT( "SE", PUT(2.2, 6.3) );
59.      CALL SYMPUT( "SM", PUT(2.46, 6.3) );
60.      run;
61.      %END;
62.      %macro cullu;
63.      LLU = MEAN - Z * SQRT(MVAR / N);
64.      mu=LLU;
65.      n1=10;
66.      n2=30;
67.      k1=2.4;
68.      k2=2.0;
69.      L1=15;
70.      L2=25;
71.      if TARGET LE 101.5 then E =101.5;
72.      else E = TARGET;

73.      z1=(E-mu)*sqrt(n1)/sigma;
74.      z2=(98.5-mu)*sqrt(n1)/sigma;
75.      chil=probchi((n1-1)*L1**2/(k1*sigma)**2, n1-1);
76.      int1=(probnorm(z1)-probnorm(z2))*chil;
77.      t=1;
78.      h=0.05;
79.      int2=0;
80.      do x=E to (E+15-h) by h;
81.      x1=(x-mu)*sqrt(n1)/sigma;
82.      x2=(x+h-mu)*sqrt(n1)/sigma;
83.      chi2=(n1-1)*(E+15-x-h/2)**2/(k1*sigma)**2;
84.      int2=int2+(probnorm(x2)-probnorm(x1))*probchi(chi2, n1-1);
85.      end;

86.      int3=0;
87.      do x=(98.5-15) to (98.5-h) by h;
88.      x1=(x-mu)*sqrt(n1)/sigma;
89.      x2=(x+h-mu)*sqrt(n1)/sigma;
90.      chi3=(n1-1)*(15-98.5+x+h/2)**2/(k1*sigma)**2;
91.      int3=int3+(probnorm(x2)-probnorm(x1))*probchi(chi3, n1-1);
92.      end;

93.      P1=int1+int2+int3;

94.      zz1=(E-mu)*sqrt(n2)/sigma;
95.      zz2=(98.5-mu)*sqrt(n2)/sigma;
96.      cchil=probchi((n2-1)*L1**2/(k2*sigma)**2, n2-1);
97.      iint1=(probnorm(zz1)-probnorm(zz2))*cchil;
98.      iint2=0;
99.      do xx=E to (E+15-h) by h;
100.     xx1=(xx-mu)*sqrt(n2)/sigma;

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```

101.     xx2=(xx+h-mu)*sqrt(n2)/sigma;
102.     cchi2=(n2-1)*(E+15-xx-h/2)**2/(k2*sigma)**2;
103.     iint2=iint2+(probnorm(xx2)-probnorm(xx1))*probchi(cchi2,
n2-1);
104.     end;

105.     iint3=0;
106.     do xx=(98.5-15) to (98.5-h) by h;
107.         xx1=(xx-mu)*sqrt(n2)/sigma;
108.         xx2=(xx+h-mu)*sqrt(n2)/sigma;
109.         cchi3=(n2-1)*(15-98.5+xx+h/2)**2/(k2*sigma)**2;
110.         iint3=iint3+(probnorm(xx2)-probnorm(xx1))*probchi(cchi3,
n2-1);
111.     end;

112.     P2a=iint1+iint2+iint3;

113.     zzz1=(123.5-mu)/sigma;
114.     if TARGET LE 101.5 then zzz2=(101.5-25-mu)/sigma;
115.     else zzz2 = (TARGET-25-mu)/sigma;

116.     P2b=(probnorm(zzz2)-probnorm(zzz1))**30;

117.     P2=max(0, P2a+P2b-1);

118.     overbdl=max(P1, P2);

119.     %MEND cullu;

120.     %MACRO cuulu;
121.     ULU = MEAN + Z * SQRT(MVAR / N);
122.     mu=ULU;
123.     n1=10;
124.     n2=30;
125.     k1=2.4;
126.     k2=2.0;
127.     L1=15;
128.     L2=25;
129.     if TARGET LE 101.5 then E =101.5;
130.     else E = TARGET;

131.     z1=(E-mu)*sqrt(n1)/sigma;
132.     z2=(98.5-mu)*sqrt(n1)/sigma;
133.     chil=probchi((n1-1)*L1**2/(k1*sigma)**2, n1-1);
134.     int1=(probnorm(z1)-probnorm(z2))*chil;
135.     t=1;
136.     h=0.05;
137.     int2=0;
138.     do x=E to (E+15-h) by h;
139.         x1=(x-mu)*sqrt(n1)/sigma;
140.         x2=(x+h-mu)*sqrt(n1)/sigma;
141.         chi2=(n1-1)*(E+15-x-h/2)**2/(k1*sigma)**2;
142.         int2=int2+(probnorm(x2)-probnorm(x1))*probchi(chi2, n1-1);
143.     end;

144.     int3=0;

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```

145.    do x=(98.5-15) to (98.5-h) by h;
146.    x1=(x-mu)*sqrt(n1)/sigma;
147.    x2=(x+h-mu)*sqrt(n1)/sigma;
148.    chi3=(n1-1)*(15-98.5+x+h/2)**2/(k1*sigma)**2;
149.    int3=int3+(probnorm(x2)-probnorm(x1))*probchi(chi3, n1-1);
150.    end;

151.    P1=int1+int2+int3;

152.    zz1=(E-mu)*sqrt(n2)/sigma;
153.    zz2=(98.5-mu)*sqrt(n2)/sigma;
154.    cchi1=probchi((n2-1)*L1**2/(k2*sigma)**2, n2-1);
155.    iint1=(probnorm(zz1)-probnorm(zz2))*cchi1;
156.    iint2=0;
157.    do xx=E to (E+15-h) by h;
158.    xx1=(xx-mu)*sqrt(n2)/sigma;
159.    xx2=(xx+h-mu)*sqrt(n2)/sigma;
160.    cchi2=(n2-1)*(E+15-xx-h/2)**2/(k2*sigma)**2;
161.    iint2=iint2+(probnorm(xx2)-probnorm(xx1))*probchi(cchi2,
n2-1);
162.    end;

163.    iint3=0;
164.    do xx=(98.5-15) to (98.5-h) by h;
165.    xx1=(xx-mu)*sqrt(n2)/sigma;
166.    xx2=(xx+h-mu)*sqrt(n2)/sigma;
167.    cchi3=(n2-1)*(15-98.5+xx+h/2)**2/(k2*sigma)**2;
168.    iint3=iint3+(probnorm(xx2)-probnorm(xx1))*probchi(cchi3,
n2-1);
169.    end;

170.    P2a=iint1+iint2+iint3;

171.    zzz1=(123.5-mu)/sigma;
172.    if TARGET LE 101.5 then zzz2=(101.5-25-mu)/sigma;
173.    else zzz2 = (TARGET-25-mu)/sigma;

174.    P2b=(probnorm(zzz2)-probnorm(zzz1))**30;

175.    P2=max(0, P2a+P2b-1);

176.    overbdu=max(P1, P2);

177.    %mend cuulu;

178.    %MACRO CALCUSP2;
179.    DATA TABC;
180.    D=&D1;
181.    Z = PROBIT((1 + SQRT(&CILEVEL/100))/2);
182.    NN = &NUM;
183.    L = &LOC;
184.    N = NN*L;
185.    CALL SYMPUT("TOT",PUT(N, 5.0));
186.    CHIERR = CINV(1 - SQRT(&CILEVEL / 100), L*(NN - 1));
187.    CHILOC = CINV(1 - SQRT(&CILEVEL / 100), L-1);
188.    SEBOUND = 9.2;

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189.     SMLIM = 9.2;
190.     NEXTL = 84.9;
191.     NEXTU = 115.1;
192.     DO SE = D TO SEBOUND BY D;
193.     MEANL = NEXTL;
194.     MEANU = NEXTU;
195.     SMBOUND = SMLIM;
196.     SE2 = SE * SE;
197.     H2 = L * (NN - 1) / CHIERR - 1;
198.     SEC = ((1 - 1/NN)*H2*SE2)**2;
199.     DO SM = D TO SMBOUND BY D;
200.     IF MEANL = . THEN GOTO OVER;
201.     SL2 = SM * SM * NN;
202.     SL2UB = (L - 1) * SL2 / CHILOC;
203.     H1 = (L - 1) / CHILOC - 1;
204.     FIRST = ((1 / NN)*H1*SL2)**2;
205.     PTEST = (1 / NN) * SL2 + (1 - 1/NN) * SE2;
206.     VAR = PTEST + SQRT(FIRST + SEC);
207.     MVAR = SL2UB;
208.     SIGMA = SQRT(VAR);
209.     DO MEAN = MEANL - D TO 115.5 BY D;
210.     %cullu
211.     IF OVERBDL > &LBOUND/100 THEN DO;
212.     MEANL = MEAN;
213.     GOTO UPPER;
214.     END;
215.     END;
216.     MEANL = .;
217.     MEANU = .;
218.     IF SE=D THEN DO;
219.     SMLIM = SM - D;
220.     OUTPUT;
221.     SM=10;
222.     GOTO OVER;
223.     1. END;
224.     IF SM=D THEN DO; SE = 10; GOTO OVER; END;
225.     GOTO SKIP;
226.     UPPER:
227.
228.     DO MEAN = MEANU + D TO 84.9 BY -D;
229.     %cuulu
230.     IF OVERBDU > &LBOUND/100 THEN DO;
231.     MEANU = MEAN;
232.     GOTO OUT;
233.     END;
234.     END;
235.     OUT:
236.     IF MEANU <= MEANL OR MEAN <= MEANL THEN DO;
237.     MEANL = .;
238.     MEANU = .;
239.     IF SE=D THEN DO;
240.     SMLIM = SM - D;
241.     OUTPUT;
242.     SM=10;
243.     GOTO OVER;
244.     END;
245.     IF SM=D THEN DO; SE = 10; GOTO OVER; END;

```

```

244.      END;

245.      SKIP: OUTPUT;
246.      IF SM = D THEN DO;
247.          NEXTL = MEANL;
248.          NEXTU = MEANU;
249.      a. END;
249.      OVER:
250.      END;
251.      END;
252.      KEEP N NN L D MEAN SE SM MEANL MEANU OVERBDL OVERBDU;
253.      data tabc;
254.      set tabc;
255.      if SE = 10 or SM = 10 then delete;
256.      run;
257.      PROC SORT DATA=TABC; BY SE SM;run;

258.      %MEND CALCUSP2;

259.      %MACRO PRTCUSP2;
260.      options ls=132;
261.      PROC TRANSPOSE DATA = TABC OUT = LDAT PREFIX = L;
262.      VAR MEANL;
263.      BY SE;

264.      PROC TRANSPOSE DATA = TABC OUT = UDAT PREFIX = U;
265.      VAR MEANU;
266.      BY SE;

267.      DATA together;
268.      MERGE LDAT UDAT;
269.      BY SE;
270.      proc sort data=together; by se;
271.      data miss;
272.      l1=.; u1=.;
273.      l2=.; u2=.;
274.      l3=.; u3=.;
275.      l4=.; u4=.;
276.      l5=.; u5=.;
277.      l6=.; u6=.;
278.      l7=.; u7=.;
279.      l8=.; u8=.;
280.      l9=.; u9=.;
281.      l10=.; u10=.;
282.      l11=.; u11=.;
283.      l12=.; u12=.;
284.      l13=.; u13=.;
285.      l14=.; u14=.;
286.      l15=.; u15=.;
287.      l16=.; u16=.;
288.      l17=.; u17=.;
289.      l18=.; u18=.;
290.      l19=.; u19=.;
291.      l20=.; u20=.;
292.      l21=.; u21=.;
293.      l22=.; u22=.;
294.      l23=.; u23=.;

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295.      124=. ; u24=. ;
296.      125=. ; u25=. ;
297.      126=. ; u26=. ;
298.      127=. ; u27=. ;
299.      128=. ; u28=. ;
300.      129=. ; u29=. ;
301.      130=. ; u30=. ;
302.      131=. ; u31=. ;
303.      132=. ; u32=. ;
304.      133=. ; u33=. ;
305.      134=. ; u34=. ;
306.      135=. ; u35=. ;
307.      136=. ; u36=. ;
308.      137=. ; u37=. ;
309.      138=. ; u38=. ;
310.      139=. ; u39=. ;
311.      140=. ; u40=. ;
312.      141=. ; u41=. ;
313.      142=. ; u42=. ;
314.      143=. ; u43=. ;
315.      144=. ; u44=. ;
316.      145=. ; u45=. ;
317.      146=. ; u46=. ;
318.      147=. ; u47=. ;
319.      148=. ; u48=. ;
320.      149=. ; u49=. ;
321.      150=. ; u50=. ;
322.      151=. ; u51=. ;
323.      152=. ; u52=. ;
324.      153=. ; u53=. ;
325.      154=. ; u54=. ;
326.      155=. ; u55=. ;
327.      156=. ; u56=. ;
328.      157=. ; u57=. ;
329.      158=. ; u58=. ;
330.      159=. ; u59=. ;
331.      160=. ; u60=. ;
332.      161=. ; u61=. ;
333.      162=. ; u62=. ;
334.      163=. ; u63=. ;
335.      164=. ; u64=. ;
336.      165=. ; u65=. ;
337.      166=. ; u66=. ;
338.      167=. ; u67=. ;
339.      168=. ; u68=. ;
340.      169=. ; u69=. ;
341.      170=. ; u70=. ;
342.      171=. ; u71=. ;
343.      172=. ; u72=. ;
344.      data all;
345.      merge miss together;
346.      DATA _NULL_;
347.      SET ALL;
348.      IF L1 EQ . THEN RETURN;
349.      FILE PRINT HEADER = TOP;
350.      PUT @1 SE 3.1 +1
351.      (L1 U1 L2 U2 L3 U3 L4 U4 L5 U5 L6 U6 L7 U7 L8 U8 L9 U9)

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352.      (5.1 +1 5.1 +2);
353.      RETURN;
354.      TOP: PUT / @9 '0.1' +10 '0.2' +10 '0.3' +10 '0.4' +10 '0.5'
+10
          i. '0.6' +10 '0.7' +10 '0.8' +10 '0.9' //
          ii. @1 'SE' @7 'LL' @12 'UL' @20 'LL' @25 'UL' @33 'LL'
          iii. @38 'UL' @46 'LL' @51 'UL' @59 'LL' @64 'UL' @72 'LL'
          iv. @77 'UL' @85 'LL' @90 'UL' @98 'LL' @103 'UL'
          v. @111 'LL' @116 'UL' //;
355.      RETURN;
356.      TITLE1 "ACCEPTANCE LIMITS FOR CONTENT UNIFORMITY";
357.      TITLE2 "SAMPLING PLAN 2";
358.      TITLE3 "TARGET=&T, LOWER BOUND = &LBOUND, CONFIDENCE LEVEL
= &CILEVEL";
359.      TITLE4 "TABLE ENTRIES ARE LOWER(LL) AND UPPER(UL) LIMITS ON
THE MEAN";
360.      TITLE5 "OF &TOT ASSAYS-&NUM ASSAYS AT EACH OF &LOC
DIFFERENT LOCATIONS";
361.      TITLE6 'SE IS THE POOLED WITHIN LOCATION STANDARD
DEVIATION';
362.      TITLE7 'STANDARD DEVIATIONS AND MEANS ARE EXPRESSED IN %
CLAIM';
363.      TITLE9 'STANDARD DEVIATION OF LOCATION MEANS';

364.      DATA _NULL_;
365.      SET ALL;
366.      IF L10 EQ . THEN RETURN;
367.      FILE PRINT HEADER = TOP;
368.      PUT @1 SE 3.1 +1
369.      (L10 U10 L11 U11 L12 U12 L13 U13 L14 U14
370.      L15 U15 L16 U16 L17 U17 L18 U18)
371.      (5.1 +1 5.1 +2);
372.      RETURN;
373.      TOP: PUT / @9 '1.0' +10 '1.1' +10 '1.2' +10 '1.3' +10 '1.4'
+10
          i. '1.5' +10 '1.6' +10 '1.7' +10 '1.8' //
          ii. @1 'SE' @7 'LL' @12 'UL' @20 'LL' @25 'UL' @33 'LL'
          iii. @38 'UL' @46 'LL' @51 'UL' @59 'LL' @64 'UL' @72 'LL'
          iv. @77 'UL' @85 'LL' @90 'UL' @98 'LL' @103 'UL'
          v. @111 'LL' @116 'UL' //;
374.      RETURN;
375.      DATA _NULL_;
376.      SET ALL;
377.      IF L19 EQ . THEN RETURN;
378.      FILE PRINT HEADER = TOP;
379.      PUT @1 SE 3.1 +1
380.      (L19 U19 L20 U20 L21 U21 L22 U22 L23 U23
381.      L24 U24 L25 U25 L26 U26 L27 U27)
382.      (5.1 +1 5.1 +2);
383.      RETURN;
384.      TOP: PUT / @9 '1.9' +10 '2.0' +10 '2.1' +10 '2.2' +10 '2.3'
+10
          i. '2.4' +10 '2.5' +10 '2.6' +10 '2.7' //
          ii. @1 'SE' @7 'LL' @12 'UL' @20 'LL' @25 'UL' @33 'LL'
          iii. @38 'UL' @46 'LL' @51 'UL' @59 'LL' @64 'UL' @72 'LL'
          iv. @77 'UL' @85 'LL' @90 'UL' @98 'LL' @103 'UL'
          v. @111 'LL' @116 'UL' //;

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385. RETURN;
386. DATA _NULL_;
387. SET ALL;
388. IF L28 = . THEN RETURN;
389. FILE PRINT HEADER = TOP;
390. PUT @1 SE 3.1 +1
391. (L28 U28 L29 U29 L30 U30 L31 U31 L32 U32
392. L33 U33 L34 U34 L35 U35 L36 U36)
393. (5.1 +1 5.1 +2);
394. RETURN;
395. TOP: PUT / @9 '2.8' +10 '2.9' +10 '3.0' +10 '3.1' +10 '3.2'
+10
      i. '3.3' +10 '3.4' +10 '3.5' +10 '3.6' //
      ii. @1 'SE' @7 'LL' @12 'UL' @20 'LL' @25 'UL' @33 'LL'
      iii. @38 'UL' @46 'LL' @51 'UL' @59 'LL' @64 'UL' @72 'LL'
      iv. @77 'UL' @85 'LL' @90 'UL' @98 'LL' @103 'UL'
      v. @111 'LL' @116 'UL' //;
396. RETURN;
397. DATA _NULL_;
398. SET ALL;
399. IF L37 EQ . THEN RETURN;
400. FILE PRINT HEADER = TOP;
401. PUT @1 SE 3.1 +1
402. (L37 U37 L38 U38 L39 U39 L40 U40 L41 U41
403. L42 U42 L43 U43 L44 U44 L45 U45)
404. (5.1 +1 5.1 +2);
405. RETURN;
406. TOP: PUT / @9 '3.7' +10 '3.8' +10 '3.9' +10 '4.0' +10 '4.1'
+10
      i. '4.2' +10 '4.3' +10 '4.4' +10 '4.5' //
      ii. @1 'SE' @7 'LL' @12 'UL' @20 'LL' @25 'UL' @33 'LL'
      iii. @38 'UL' @46 'LL' @51 'UL' @59 'LL' @64 'UL' @72 'LL'
      iv. @77 'UL' @85 'LL' @90 'UL' @98 'LL' @103 'UL'
      v. @111 'LL' @116 'UL' //;
407. RETURN;
408. DATA _NULL_;
409. SET ALL;
410. IF L46 EQ . THEN RETURN;
411. FILE PRINT HEADER = TOP;
412. PUT @1 SE 3.1 +1
413. (L46 U46 L47 U47 L48 U48 L49 U49 L50 U50
414. L51 U51 L52 U52 L53 U53 L54 U54)
415. (5.1 +1 5.1 +2);
416. RETURN;
417. TOP: PUT / @9 '4.6' +10 '4.7' +10 '4.8' +10 '4.9' +10 '5.0'
+10
      i. '5.1' +10 '5.2' +10 '5.3' +10 '5.4' //
      ii. @1 'SE' @7 'LL' @12 'UL' @20 'LL' @25 'UL' @33 'LL'
      iii. @38 'UL' @46 'LL' @51 'UL' @59 'LL' @64 'UL' @72 'LL'
      iv. @77 'UL' @85 'LL' @90 'UL' @98 'LL' @103 'UL'
      v. @111 'LL' @116 'UL' //;
418. RETURN;
419. DATA _NULL_;
420. SET ALL;
421. IF L55 EQ . THEN RETURN;
422. FILE PRINT HEADER = TOP;
423. PUT @1 SE 3.1 +1

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424.      (L55 U55 L56 U56 L57 U57 L58 U58 L59 U59
425.      L60 U60 L61 U61 L62 U62 L63 U63)
426.      (5.1 +1 5.1 +2);
427.      RETURN;
428.      TOP: PUT / @9 '5.5' +10 '5.6' +10 '5.7' +10 '5.8' +10 '5.9'
+10
          i. '6.0' +10 '6.1' +10 '6.2' +10 '6.3' //
          ii. @1 'SE' @7 'LL' @12 'UL' @20 'LL' @25 'UL' @33 'LL'
          iii. @38 'UL' @46 'LL' @51 'UL' @59 'LL' @64 'UL' @72 'LL'
          iv. @77 'UL' @85 'LL' @90 'UL' @98 'LL' @103 'UL'
          v. @111 'LL' @116 'UL' //;
429.      RETURN;
430.      DATA _NULL_;
431.      SET ALL;
432.      IF L64 EQ . THEN RETURN;
433.      FILE PRINT HEADER = TOP;
434.      PUT @1 SE 3.1 +1
435.      (L64 U64 L65 U65 L66 U66 L67 U67 L68 U68
436.      L69 U69 L70 U70 L71 U71 L72 U72)
437.      (5.1 +1 5.1 +2);
438.      RETURN;
439.      TOP: PUT / @9 '6.4' +10 '6.5' +10 '6.6' +10 '6.7' +10 '6.8'
+10
          i. '6.9' +10 '7.0' +10 '7.1' +10 '7.2' //
          ii. @1 'SE' @7 'LL' @12 'UL' @20 'LL' @25 'UL' @33 'LL'
          iii. @38 'UL' @46 'LL' @51 'UL' @59 'LL' @64 'UL' @72 'LL'
          iv. @77 'UL' @85 'LL' @90 'UL' @98 'LL' @103 'UL'
          v. @111 'LL' @116 'UL' //;
440.      RETURN;

441.      run;
442.      %MEND PRTCUSP2;

443.      %MACRO EVCUSP2;

444.      %MACRO SIGCUSP2;
445.      %calcusp2
446.      %DO U = &ULOW %TO &UHIGH %BY &UINCRE;
447.      %DO SIGSE = &SELOW %TO &SEHIGH %BY &SEINCRE;
a. %DO SIGSM = &SMLOW %TO &SMHIGH %BY &SMINCRE;

448.      DATA SAVE2;
449.      SET TABC END = LAST;
450.      U = &U / &UDIV;
451.      D = &D1;
452.      SIGSE = &SIGSE / &SEDIV;
453.      SIGSM = &SIGSM / &SMDIV;
454.      SIGSM2 = SIGSM * SIGSM;
455.      EXPSE2 = SIGSE * SIGSE;
456.      EXPSM2 = EXPSE2 + NN * SIGSM * SIGSM;
457.      PMEAN = PROBNORM((MEANU - U) * SQRT((N) / EXPSM2));
a. PROBNORM((MEANL - U) * SQRT((N) / EXPSM2));
458.      PSE = PROBCHI(L * (NN - 1) * SE * SE / EXPSE2, L * (NN - 1))
a. PROBCHI(L * (NN - 1) * (SE - D) * (SE - D) /
b. EXPSE2, L * (NN - 1));

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459.      PSM = PROBCHI((L - 1) * NN * SM * SM / EXPSM2, L - 1)
      a. PROBCHI((L - 1) * NN * (SM - D) * (SM - D) /
      b. EXPSM2, L - 1);
460.      P = PMEAN * PSE * PSM;
461.      PSUM + P;
462.      IF LAST THEN OUTPUT;
463.      RUN;
464.      PROC APPEND BASE = SAVES2E DATA = SAVE2;
465.      RUN;

      a. %END;
466.      %END;
467.      %END;

468.      %MEND SIGCUSP2;

469.      %SIGCUSP2

470.      PROC PRINT DATA = SAVES2E split = '*';
471.      label U = 'MEAN'
      a. SIGSE = 'WITHIN LOCATION*STD DEV'
      b. SIGSM = 'BETWEEN LOCATION* STD DEV'
      c. PSUM = 'PROBABILITY*OF*PASSING';
472.      VAR U SIGSE SIGSM PSUM;
473.      TITLE1 "ACCEPTANCE LIMITS FOR CONTENT UNIFORMITY";
474.      TITLE2 'SAMPLING PLAN 2';
475.      TITLE3 "PROBABILITY OF PASSING ACCEPTANCE LIMIT TABLE";
476.      TITLE4 "WITH &NUM ASSAYS AT EACH OF &LOC LOCATIONS";
477.      TITLE5 "CONFIDENCE LEVEL = &CILEVEL & LOWER BOUND =
      &LBOUND";
478.      RUN;
479.      %MEND EVCUSP2;

480.      %MACRO SMPCUSP2;

481.      DATA TAB;
482.      Z = PROBIT((1 + SQRT(&CILEVEL/100))/2);
483.      NN = &NUM;
484.      L = &LOC;
485.      N = NN*L;
486.      SE = &SE;
487.      SM = &SM;
488.      MEAN = &MEAN;
489.      CILEVEL = &CILEVEL;
490.      CHIERR = CINV(1 - SQRT(&CILEVEL / 100), L*(NN - 1));
491.      CHILOC = CINV(1 - SQRT(&CILEVEL / 100), L-1);
492.      SE2 = SE * SE;
493.      H2 = L * (NN - 1) / CHIERR - 1;
494.      SEC = ((1 - 1/NN)*H2*SE2)**2;
495.      SL2 = SM * SM * NN;
496.      SL2UB = (L - 1) * SL2 / CHILOC;
497.      H1 = (L - 1) / CHILOC - 1;
498.      FIRST = ((1 / NN)*H1*SL2)**2;
499.      PTEST = (1 / NN) * SL2 + (1 - 1/NN) * SE2;
500.      VAR = PTEST + SQRT(FIRST + SEC);
501.      MVAR = SL2UB;
502.      SIGMA = SQRT(VAR);

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```

503.      %cullu
504.      %cuulu
505.      OVERBD = MIN(OVERBDU, OVERBDL);
506.      KEEP SE MEAN SM OVERBD;
507.      PROC PRINT SPLIT='*';
508.      LABEL    SE = 'SAMPLE*WITHIN LOCATION*STD DEV'
      a. MEAN = 'SAMPLE*MEAN'
      b. SM = 'SAMPLE*BETWEEN LOCATION*STD DEV'
      c. OVERBD = 'LOWER BOUND';
509.      ID MEAN;
510.      VAR SE SM OVERBD;
511.      TITLE1 "ACCEPTANCE LIMITS FOR CONTENT UNIFORMITY";
512.      TITLE2 "SAMPLING PLAN 2 (&LOC LOCATIONS, &NUM PER
LOCATION)";
513.      TITLE3 "PROPORTION OF FUTURE SAMPLES PASSING THE USP TEST";
514.      TITLE4 "WITH &CILEVEL.% ASSURANCE";
515.      TITLE5 'FOR GIVEN SAMPLE MEAN, WITHIN AND BETWEEN LOCATION
STD DEV';
516.      RUN;
517.      %MEND SMPCUSP2;

518.      %MACRO ANACUSP2;

519.      %IF %UPCASE(&A1CUSP2)=Y %THEN %DO;
520.      %CALCUSP2;
521.      %PRTCUSP2;
522.      %END;
523.      %IF %UPCASE(&A2CUSP2)=Y %THEN %DO;
524.      %EVCUSP2;
525.      PROC DATASETS LIBRARY=WORK;
526.      DELETE SAVES2E;
527.      %END;
528.      %IF %UPCASE(&A3CUSP2)=Y %THEN %DO;
529.      %SMPCUSP2;
530.      %END;
531.      %MEND ANACUSP2;

532.      %ANACUSP2

533.      RUN;
534.      %MEND CUSP2;
535.      %CUSP2

```


DISP1.SAS

```
1. %MACRO DISP1(A1DISP1=,
2. A2DISP1=,
3. A3DISP1=);

4. data _null_;
5. set mdisp1;
6. CALL SYMPUT( "Q", PUT(LQ, 4.1));
7. CALL SYMPUT( "NUMBER", PUT(LNUMBER, 4.0));
8. CALL SYMPUT( "LBOUND", PUT(LLBOUND, 4.1));
9. CALL SYMPUT( "CILEVEL", PUT(LCILEVEL, 4.1));
10. run;

11. %IF %UPCASE(&A2DISP1)=Y %THEN %DO;
12. data _null_;
13. set ev1;
14. CALL SYMPUT( "ULOW", PUT(LULOW, 4.0));
15. CALL SYMPUT( "UHIGH", PUT(LUHIGH, 4.0));
16. CALL SYMPUT( "UINCRE", PUT(LUINCRE, 4.0));
17. CALL SYMPUT( "UDIV", PUT(LUDIV, 4.0));
18. CALL SYMPUT( "CVLOW", PUT(LCVLOW, 4.0));
19. CALL SYMPUT( "CVHIGH", PUT(LCVHIGH, 4.0));
20. CALL SYMPUT( "CVINCRE", PUT(LCVINCRE, 4.0));
21. CALL SYMPUT( "CVDIV", PUT(LCVDIV, 4.0));
22. RUN;
23. %END;
24. %ELSE %IF %UPCASE(&A2DISP1)=N %THEN %DO;
25. data _null_;
26. CALL SYMPUT( "ULOW", PUT(950, 4.0));
27. CALL SYMPUT( "UHIGH", PUT(1000, 4.0));
28. CALL SYMPUT( "UINCRE", PUT(50, 4.0));
29. CALL SYMPUT( "UDIV", PUT(10, 4.0));
30. CALL SYMPUT( "CVLOW", PUT(10, 4.0));
31. CALL SYMPUT( "CVHIGH", PUT(40, 4.0));
32. CALL SYMPUT( "CVINCRE", PUT(30, 4.0));
33. CALL SYMPUT( "CVDIV", PUT(10, 4.0));
34. RUN;
35. %END;

36. %IF %UPCASE(&A3DISP1)=Y %THEN %DO;
37. data _null_;
38. set smp1;
39. CALL SYMPUT( "MEAN", PUT(LMEAN, 6.2));
40. CALL SYMPUT( "CV", PUT(LCV, 6.2));
41. CALL SYMPUT( "LCV", PUT(LCV, 6.2));
42. run;
43. %END;
44. %ELSE %IF %UPCASE(&A3DISP1)=N %THEN %DO;
45. data _null_;
46. CALL SYMPUT( "MEAN", PUT(100, 6.2));
47. CALL SYMPUT( "CV", PUT(4, 6.2));
48. CALL SYMPUT( "LCV", PUT(4, 6.2));
49. run;
50. %END;
```

```

51.      %MACRO COMPUTE;
52.      F1 = (1 - PROBNORM((5 - LLU)/SIGMA)) ** 6;
53.      SN2 = SQRT(12);
54.      PM2 = PROBNORM (SN2 * -LLU / SIGMA);
55.      PB2 = 1 - PROBNORM ((-15 - LLU) / SIGMA);
56.      F2 = PB2 ** 12 - PM2;
57.      SN3 = SQRT(24);
58.      PM3 = PROBNORM (SN3 * -LLU / SIGMA);
59.      P2 = PROBNORM ((-15 - LLU) / SIGMA) - PROBNORM ((-25 - LLU)
/ SIGMA);
60.      P3 = 1 - PROBNORM ((-15 - LLU) / SIGMA);
61.      F3 = P3**24 + 24*P2*P3**23 + 276*P2*P2*P3**22 - PM3;
62.      OVERBD = MAX(F1, F2, F3);
63.      %mend compute;
64.      %MACRO CALDISP1;
65.      DATA D1ONE;
66.      Q = &Q;
67.      LIM = 100 - Q;
68.      N = &NUMBER;
69.      D=0.2;
70.      Z = PROBIT(SQRT(&CILEVEL / 100));
71.      CHI = CINV(1 - SQRT(&CILEVEL / 100),N - 1);
72.      STARTSD = 0.002;
73.      DO MEANADJ = D TO LIM BY D;
74.      BEGIN = STARTSD;
75.      DO SAMPSD = BEGIN TO 60.0 BY 0.001;
76.      SIGMA = SQRT((N - 1) * SAMPSD * SAMPSD / CHI);
77.      LLU = MEANADJ - Z *SIGMA / SQRT(N);
78.      %COMPUTE
79.      IF OVERBD < &LBOUND/100 AND SAMPSD <= 0.00201 then do;
80.      CV = 0; OUTPUT; SAMPLSD = 65.0; GOTO NEXT; END;
81.      IF OVERBD < &LBOUND/100 THEN DO;
82.      SAMPSD = SAMPSD - 0.001;
83.      STARTSD = SAMPSD;
84.      MEAN = MEANADJ + Q;
85.      CV = 100 * SAMPSD / MEAN;
      a. OUTPUT;
      b. SAMPSD = 65.0;
      c. END;
86.      NEXT;
87.      END;
88.      END;
89.      KEEP CV MEAN ;
90.      PROC SORT DATA=D1ONE; BY MEAN;
91.      DATA
92.      ONE(RENAME = (MEAN = X1 CV = CV1))
93.      TWO(RENAME = (MEAN = X2 CV = CV2))
94.      THREE(RENAME = (MEAN = X3 CV = CV3))
95.      FOUR(RENAME = (MEAN = X4 CV = CV4))
96.      FIVE(RENAME = (MEAN = X5 CV = CV5));
97.      SET D1ONE;
98.      Q = &Q;
99.      LIM = 100 - Q;
100.     IF Q < MEAN <= Q+ LIM/5 + 0.0001 THEN
      OUTPUT ONE;

```

```

101.      IF Q+LIM/5 + 0.0001 < MEAN <= Q+ 2*LIM/5 + 0.0001 THEN
      OUTPUT TWO;
102.      IF Q+2*LIM/5 + 0.0001 < MEAN <= Q+ 3*LIM/5 + 0.0001 THEN
      OUTPUT THREE;
103.      IF Q+3*LIM/5 + 0.0001 < MEAN <= Q+ 4*LIM/5 + 0.0001 THEN
      OUTPUT FOUR;
104.      IF Q+4*LIM/5 + 0.0001 < MEAN <= Q+ LIM + 0.0001 THEN
      OUTPUT FIVE;
105.      DATA D1ALL;
106.      MERGE ONE TWO THREE FOUR FIVE;
107.      RUN;

108.      %MEND CALDISP1;

109.      %MACRO PRTDISP1;
110.      OPTIONS MISSING = ' ' NODATE NONUMBER;
111.      OPTIONS LS=132;
112.      PROC PRINT DATA=D1ALL SPLIT = '*';
113.      FORMAT CV1 CV2 CV3 CV4 CV5 5.2;
114.      LABEL
      a. X1 = ' MEAN*(% CLAIM)'
      b. X2 = ' MEAN*(% CLAIM)'
      c. X3 = ' MEAN*(% CLAIM)'
      d. X4 = ' MEAN*(% CLAIM)'
      e. X5 = ' MEAN*(% CLAIM)'
      f. CV1 = 'CV*(%)'
      g. CV2 = 'CV*(%)'
      h. CV3 = 'CV*(%)'
      i. CV4 = 'CV*(%)'
      j. CV5 = 'CV*(%)';
115.      VAR CV1 X2 CV2 X3 CV3 X4 CV4 X5 CV5;
116.      ID X1;
117.      TITLE "ACCEPTANCE LIMITS FOR DISSOLUTION (N = &NUMBER, Q =
      &Q)";
118.      TITLE2 'SAMPLING PLAN 1';
119.      TITLE3 "(MEETING LIMITS GUARANTEES WITH &CILEVEL %
      ASSURANCE, ";
120.      TITLE4 "THAT AT LEAST &LBOUND% OF ALL FUTURE SAMPLES
      TESTED";
121.      TITLE5 'FOR DISSOLUTION WILL PASS THE USP TEST)';
122.      TITLE6 "TABLE ENTRY IS UPPER LIMIT ON CV OF &NUMBER
      DISSOLUTION ASSAYS";
123.      %MEND PRTDISP1;

124.      %MACRO EVDISP1;

125.      DATA DIONE;
126.      SET d1one;
127.      x = mean;
128.      std = x*cv/100;
129.      N = &NUMBER;

130.      %MACRO SIGDISP1;

131.      %DO CV = &CVLOW %TO &CVHIGH %BY &CVINCRE;

```

```

132.      %DO U = &ULOW %TO &UHIGH %BY &UINCRE;

      a. DATA D1SAVE;
          i. SET DIONE END = LAST;
          ii. U = &U / &UDIV;
          iii. CV = &CV / &CVDIV;
          iv. SIGMA = U * CV / 100;
          v. PMEAN = PROBNORM((X - U) * SQRT(N) / SIGMA)
      b. PROBNORM((LAG(X) - U) * SQRT(N) / SIGMA);
          i. AVEHT = (STD + LAG(STD)) / 2;
          ii. PSTD = PROBCHI((N - 1) * AVEHT * AVEHT
              1. / (SIGMA * SIGMA), N - 1);
          iii. PT = PMEAN * PSTD ;
          iv. PTRAP + PT;
          v. IF X > 99.9 THEN DO;
          vi. PMEAN = 1 - PROBNORM((X - U) * SQRT (N) / SIGMA);
          vii. PSTD = PROBCHI((N - 1) * STD * STD
              a. / (SIGMA * SIGMA), N - 1);
          viii. PT = PMEAN * PSTD;
          ix. PTRAP + PT;
          x. END;
          xi. IF LAST THEN OUTPUT;
      c. RUN;

133.      PROC APPEND BASE = D1SAVALL DATA = D1SAVE;

      a. %END;

134.      %END;

135.      %MEND SIGDISP1;

136.      %SIGDISP1

137.      PROC PRINT DATA = D1SAVALL split = '*';
138.      label ptrap = 'PROBABILITY*OF*PASSING';
139.      VAR CV PTRAP;
140.      ID U;
141.      TITLE "ACCEPTANCE LIMITS FOR DISSOLUTION (N = &NUMBER, Q =
          &Q)";
142.      TITLE2 'SAMPLING PLAN 1';
143.      TITLE3 'PROBABILITY OF PASSING ACCEPTANCE LIMIT TABLE';
144.      TITLE4 "CONFIDENCE LEVEL = &CILEVEL AND LOWER BOUND =
          &LBOUND";
145.      RUN;
146.      %MEND EVDISP1;

147.      %MACRO SMPDISP1;

148.      DATA DI1SMP;
149.      LABEL OVERBD = 'OVERALL LOWER BOUND'
      a. MEAN = 'SAMPLE MEAN(%CLAIM)';
150.      Q = &Q;
151.      N = &NUMBER;
152.      CILEVEL = &CILEVEL;
153.      Z = PROBIT(SQRT(&CILEVEL / 100));
154.      N = &NUMBER;
155.      CHI = CINV(1 - SQRT(&CILEVEL / 100), N - 1);

```

```

156.     MEAN = &MEAN;
157.     MEANADJ = MEAN - Q;
158.     CV = &LCV;
159.     SAMPSD= &MEAN * CV/100;
160.     SIGMA = SQRT((N - 1) * SAMPSD * SAMPSD / CHI);
161.     LLU = MEANADJ - Z *SIGMA / SQRT(N);
162.     %COMPUTE
163.     PROC PRINT SPLIT = '*';
164.     LABEL SAMPSD = 'SAMPLE*STD DEV*(% CLAIM)'
      a. MEAN = 'SAMPLE* MEAN*(% CLAIM)'
      b. OVERBD = 'LOWER BOUND';

165.     ID MEAN;
166.     VAR SAMPSD CV OVERBD;
167.     TITLE "ACCEPTANCE LIMITS FOR DISSOLUTION (N = &NUMBER, Q =
      &Q)";
168.     TITLE2 'SAMPLING PLAN 1';
169.     TITLE3 "PROPORTION OF FUTURE SAMPLES PASSING THE USP TEST";
170.     TITLE4 "FOR A GIVEN SAMPLE MEAN AND CV WITH &CILEVEL.%
      ASSURANCE";
171.     run;
172.     %MEND SMPDISP1;

173.     %MACRO ANADISP1;

174.     %IF %UPCASE(&A1DISP1)=Y OR %UPCASE(&A2DISP1)=Y %THEN %DO;
175.     %CALDISP1;
176.     %END;
177.     %IF %UPCASE(&A1DISP1)=Y %THEN %DO;
178.     %PRTDISP1;
179.     %END;
180.     %IF %UPCASE(&A2DISP1)=Y %THEN %DO;
181.     %EVDISP1;
182.     PROC DATASETS LIBRARY = WORK;
183.     DELETE D1SAVALL;
184.     %END;
185.     %IF %UPCASE(&A3DISP1)=Y %THEN %DO;
186.     %SMPDISP1;
187.     %END;
188.     %MEND ANADISP1;

189.     %ANADISP1
190.     RUN;
191.     %MEND DISP1;
192.     %DISP1

```

DISP2.SAS - No Changes or Additions

```
1. %MACRO DISP2(A1DISP2=,
2. A2DISP2=,
3. A3DISP2=);
4. OPTIONS NODATE NONUMBER;

5. data _null_;
6. set mdisp2;
7. CALL SYMPUT("Q", PUT(LQ, 4.1));
8. CALL SYMPUT("DSE", PUT(LDSE, 4.2));
9. CALL SYMPUT("DSM", PUT(LDSM, 4.2));
10. CALL SYMPUT("LOC", PUT(LLOC, 4.0));
11. CALL SYMPUT("NUM", PUT(LNUM, 4.0));
12. CALL SYMPUT("LBOUND", PUT(LLBOUND, 4.1));
13. CALL SYMPUT("CILEVEL", PUT(LCILEVEL, 4.1));
14. run;

15. %IF %UPCASE(&A2DISP2)=Y %THEN %DO;
16. data _null_;
17. set ev2;
18. CALL SYMPUT("ULOW", PUT(LULOW, 4.0));
19. CALL SYMPUT("UHIGH", PUT(LUHIGH, 4.0));
20. CALL SYMPUT("UINCRE", PUT(LUINCRE, 4.0));
21. CALL SYMPUT("UDIV", PUT(LUDIV, 4.0));
22. CALL SYMPUT("SELOW", PUT(LSELOW, 4.0));
23. CALL SYMPUT("SEHIGH", PUT(LSEHIGH, 4.0));
24. CALL SYMPUT("SEINCRE", PUT(LSEINCRE, 4.0));
25. CALL SYMPUT("SEDIV", PUT(LSEDIV, 4.0));
26. CALL SYMPUT("SMLow", PUT(LSMLow, 4.0));
27. CALL SYMPUT("SMHIGH", PUT(LSMHIGH, 4.0));
28. CALL SYMPUT("SMINCRE", PUT(LSMINCRE, 4.0));
29. CALL SYMPUT("SMDIV", PUT(LSMDIV, 4.0));
30. RUN;
31. %END;
32. %ELSE %IF %UPCASE(&A2DISP2)=N %THEN %DO;
33. data _null_;
34. CALL SYMPUT("ULOW", PUT(950, 4.0));
35. CALL SYMPUT("UHIGH", PUT(1000, 4.0));
36. CALL SYMPUT("UINCRE", PUT(50, 4.0));
37. CALL SYMPUT("UDIV", PUT(10, 4.0));
38. CALL SYMPUT("SELOW", PUT(22, 4.0));
39. CALL SYMPUT("SEHIGH", PUT(22, 4.0));
40. CALL SYMPUT("SEINCRE", PUT(10, 4.0));
41. CALL SYMPUT("SEDIV", PUT(10, 4.0));
42. CALL SYMPUT("SMLow", PUT(22, 4.0));
43. CALL SYMPUT("SMHIGH", PUT(22, 4.0));
44. CALL SYMPUT("SMINCRE", PUT(10, 4.0));
45. CALL SYMPUT("SMDIV", PUT(10, 4.0));
46. RUN;
47. %END;

48. %IF %UPCASE(&A3DISP2)=Y %THEN %DO;
49. data _null_;
```

```

50.      set smp2;
51.      CALL SYMPUT( "MEAN", PUT(LMEAN, 6.3));
52.      CALL SYMPUT( "SE", PUT(LSE, 6.3));
53.      CALL SYMPUT( "SM", PUT(LSM, 6.3));
54.      run;
55.      %END;
56.      %ELSE %IF %UPCASE(&A3DISP2)=N %THEN %DO;
57.      data _null_;
58.      CALL SYMPUT( "MEAN", PUT(100, 6.3));
59.      CALL SYMPUT( "SE", PUT(2.2, 6.3));
60.      CALL SYMPUT( "SM", PUT(2.46, 6.3));
61.      run;
62.      %END;

63.      %MACRO COMPUTE;
64.      F1 = (1 - PROBNORM((5 - LLU)/SIGMA)) ** 6;
65.      SN2 = SQRT(12);
66.      PM2 = PROBNORM (SN2 * -LLU / SIGMA);
67.      PB2 = 1 - PROBNORM ((-LLU - 15) / SIGMA);
68.      F2 = PB2 ** 12 - PM2;
69.      SN3 = SQRT(24);
70.      PM3 = PROBNORM (SN3 * -LLU / SIGMA);
71.      P2 = PROBNORM ((-LLU - 15) / SIGMA) - PROBNORM ((-LLU - 25)
/ SIGMA);
72.      P3 = 1 - PROBNORM ((-LLU - 15) / SIGMA);
73.      F3 = P3**24 + 24*P2*P3**23 + 276*P2*P2*P3**22 - PM3;
74.      OVERBD = MAX(F1, F2, F3);
75.      %mend compute;

76.      %MACRO CALDISP2;
77.      DATA TABD;
78.      DM =0.10;
79.      DSE = &DSE;
80.      DSM = &DSM;
81.      Q = &Q;
82.      LIM = 100 - Q;
83.      NN = &NUM;
84.      L = &LOC;
85.      N = NN*L;
86.      CALL SYMPUT( "TOT", PUT(N, 5.0));
87.      Z = PROBIT(SQRT(&CILEVEL / 100));
88.      CHIERR = CINV(1 - SQRT(&CILEVEL / 100), L*(NN - 1));
89.      CHILOC = CINV(1 - SQRT(&CILEVEL / 100), L-1);
90.      SEBOUND = 60;
91.      SMLIM = 60;
92.      NEXTM = 0.2;
93.      DO SE = DSE TO SEBOUND BY DSE;
94.      MEANL = NEXTM;
95.      SMBOUND = SMLIM;
96.      SE2 = SE * SE;
97.      H2 = L * (NN - 1) / CHIERR - 1;
98.      SEC = ((1 - 1/NN)*H2*SE2)**2;
99.      DO SM = DSM TO SMBOUND BY DSM;
100.     IF MEANL =. THEN GOTO OVER;
101.     SL2 = SM * SM * NN;

```

```

102.     SL2UB = (L - 1) * SL2 / CHILOC;
103.     H1 = (L - 1) / CHILOC - 1;
104.     FIRST = ((1 / NN)*H1*SL2)**2;
105.     PTEST = (1 / NN) * SL2 + (1 - 1/NN) * SE2;
106.     VAR = PTEST + SQRT(FIRST + SEC);
107.     MVAR = SL2UB;
108.     SIGMA = SQRT(VAR);
109.     DO MEANADJ = MEANL TO LIM BY DM;
110.     LLU = MEANADJ - Z *SQRT(MVAR / N);
111.     %COMPUTE
112.     IF OVERBD > &LBOUND/100 THEN DO;
113.     MEANL = MEANADJ;
114.     GOTO SKIP;

                                i.  END;

115.     END;
116.     MEANL = .;
117.     IF SE=DSE THEN DO;
118.     SMLIM = SM - DSM;
119.     MEAN = MEANL + Q;
120.     OUTPUT;
121.     SM = 90;
122.     GOTO OVER;
                                i.  END;
123.     IF SM=DSM THEN DO; SE = 90; GOTO OVER; END;
124.     SKIP:
125.     MEAN = MEANL + Q;
126.     OUTPUT;
127.     IF SM = DSM THEN NEXTM = MEANL;
128.     OVER:
129.     END;
130.     END;
131.     KEEP N NN L MEAN SE SM OVERBD;
132.     PROC SORT DATA=TABD; BY SE SM;

133.     %MEND CALDISP2;

134.     %MACRO PRTDISP2;
135.     options ls=132;

136.     PROC TABULATE DATA=TABD FORMAT=6.2 FORMCHAR='          ';
137.     CLASS SE SM;
138.     FORMAT SE 6.2 SM 6.2;
139.     VAR MEAN;
140.     TABLE SE, SUM*MEAN = ' ' * (SM = ' ')/rts=8;
141.     KEYLABEL SUM = 'STANDARD DEVIATION OF LOCATION MEANS';
142.     TITLE "ACCEPTANCE LIMITS FOR DISSOLUTION (Q = &Q) ";
143.     TITLE2 'SAMPLING PLAN 2';
144.     TITLE3 "LOWER BOUND = &LBOUND, CONFIDENCE LEVEL =
&CILEVEL";
145.     TITLE4 'TABLE ENTRIES ARE LOWER LIMITS ON THE MEAN';
146.     TITLE5 "OF &TOT ASSAYS-&NUM ASSAYS AT EACH OF &LOC
DIFFERENT LOCATIONS";
147.     TITLE6 'SE IS THE POOLED WITHIN LOCATION STANDARD
DEVIATION';
148.     TITLE7 'STANDARD DEVIATIONS AND MEANS ARE EXPRESSED IN %
CLAIM';

```



```

149.      run;

150.      %MEND PRTDISP2;

151.      %MACRO EVDISP2;

152.      %MACRO SIGDISP2;
153.      %CALDISP2
154.      %DO U = &ULOW %TO &UHIGH %BY &UINCRE;
155.      %DO SIGSE = &SELOW %TO &SEHIGH %BY &SEINCRE;
      a. %DO SIGSM = &SMLOW %TO &SMHIGH %BY &SMINCRE;

156.      DATA SAVE2;
157.      SET TABD END = LAST;
158.      U = &U / &UDIV;
159.      DSE = &DSE;
160.      DSM = &DSM;
161.      SIGSE = &SIGSE / &SEDIV;
162.      SIGSM = &SIGSM / &SMDIV;
163.      SIGSM2 = SIGSM * SIGSM;
164.      EXPSE2 = SIGSE * SIGSE;
165.      EXPSM2 = EXPSE2 + NN * SIGSM * SIGSM;
166.      PMEAN = 1 - PROBNORM((MEAN - U) * SQRT((N) / EXPSM2));
167.      PSE = PROBCHI(L * (NN - 1) * SE * SE / EXPSE2, L * (NN - 1))
      a. PROBCHI(L * (NN - 1) * (SE - DSE) * (SE - DSE) /
      b. EXPSE2, L * (NN - 1));
168.      PSM = PROBCHI((L - 1) * NN * SM * SM / EXPSM2, L - 1)
      a. PROBCHI((L - 1) * NN * (SM - DSM) * (SM - DSM) /
      b. EXPSM2, L - 1);
169.      P = PMEAN * PSE * PSM;
170.      PSUM + P;
171.      IF LAST THEN OUTPUT;
172.      RUN;
173.      PROC APPEND BASE = SAVES2E DATA = SAVE2;
174.      RUN;

      a. %END;
175.      %END;
176.      %END;

177.      %MEND SIGDISP2;

178.      %SIGDISP2

179.      PROC PRINT DATA = SAVES2E split = '*';
180.      label U = 'MEAN'
      a. SIGSE = 'WITHIN LOCATION*STD DEV'
      b. SIGSM = 'BETWEEN LOCATION* STD DEV'
      c. PSUM = 'PROBABILITY*OF*PASSING';
181.      VAR U SIGSE SIGSM PSUM;
182.      TITLE1 "ACCEPTANCE LIMITS FOR DISSOLUTION (Q = &Q) ";
183.      TITLE2 'SAMPLING PLAN 2';
184.      TITLE3 "PROBABILITY OF PASSING DISSOLUTION ACCEPTANCE LIMIT
TABLE";
185.      TITLE4 "WITH &NUM ASSAYS AT EACH OF &LOC LOCATIONS";

```

```

186.     TITLE5 "CONFIDENCE LEVEL = &CILEVEL & LOWER BOUND =
        &LBOUND";
187.     RUN;
188.     %MEND EVDISP2;

189.     %MACRO SMPDISP2;

190.     DATA TAB;
191.     Z = PROBIT(SQRT(&CILEVEL/100));
192.     NN = &NUM;
193.     L = &LOC;
194.     N = NN*L;
195.     SE = &SE;
196.     SM = &SM;
197.     MEAN = &MEAN;
198.     Q = &Q;
199.     MEANADJ = MEAN - Q;
200.     CILEVEL = &CILEVEL;
201.     CHIERR = CINV(1 - SQRT(&CILEVEL / 100), L*(NN - 1));
202.     CHILOC = CINV(1 - SQRT(&CILEVEL / 100), L-1);
203.     SE2 = SE * SE;
204.     H2 = L * (NN - 1) / CHIERR - 1;
205.     SEC = ((1 - 1/NN)*H2*SE2)**2;
206.     SL2 = SM * SM * NN;
207.     SL2UB = (L - 1) * SL2 / CHILOC;
208.     H1 = (L - 1) / CHILOC - 1;
209.     FIRST = ((1 / NN)*H1*SL2)**2;
210.     PTEST = (1 / NN) * SL2 + (1 - 1/NN) * SE2;
211.     VAR = PTEST + SQRT(FIRST + SEC);
212.     MVAR = SL2UB;
213.     SIGMA = SQRT(VAR);
214.     LLU = MEANADJ - Z *SQRT(MVAR / N);
215.     %COMPUTE
216.     KEEP SE MEAN SM OVERBD;
217.     PROC PRINT SPLIT='*';
218.     LABEL    SE = 'SAMPLE*WITHIN LOCATION*STD DEV'
a. MEAN = 'SAMPLE*MEAN'
b. SM = 'SAMPLE*BETWEEN LOCATION*STD DEV'
c. OVERBD = 'LOWER BOUND';
219.     ID MEAN;
220.     VAR SE SM OVERBD;
221.     TITLE "ACCEPTANCE LIMITS FOR DISSOLUTION (Q = &Q) ";
222.     TITLE2 "SAMPLING PLAN 2 (&LOC LOCATIONS, &NUM PER
        LOCATION)";
223.     TITLE3 'PROPORTION OF FUTURE SAMPLES PASSING THE USP TEST';
224.     TITLE4 "WITH &CILEVEL.% ASSURANCE";
225.     TITLE5 'GIVEN THE SAMPLE MEAN, WITHIN AND BETWEEN STD DEV';
226.     RUN;
227.     %MEND SMPDISP2;

228.     %MACRO ANADISP2;

229.     %IF %UPCASE(&A1DISP2)=Y %THEN %DO;
230.     %CALDISP2;
231.     %PRTDISP2;
232.     %END;

```

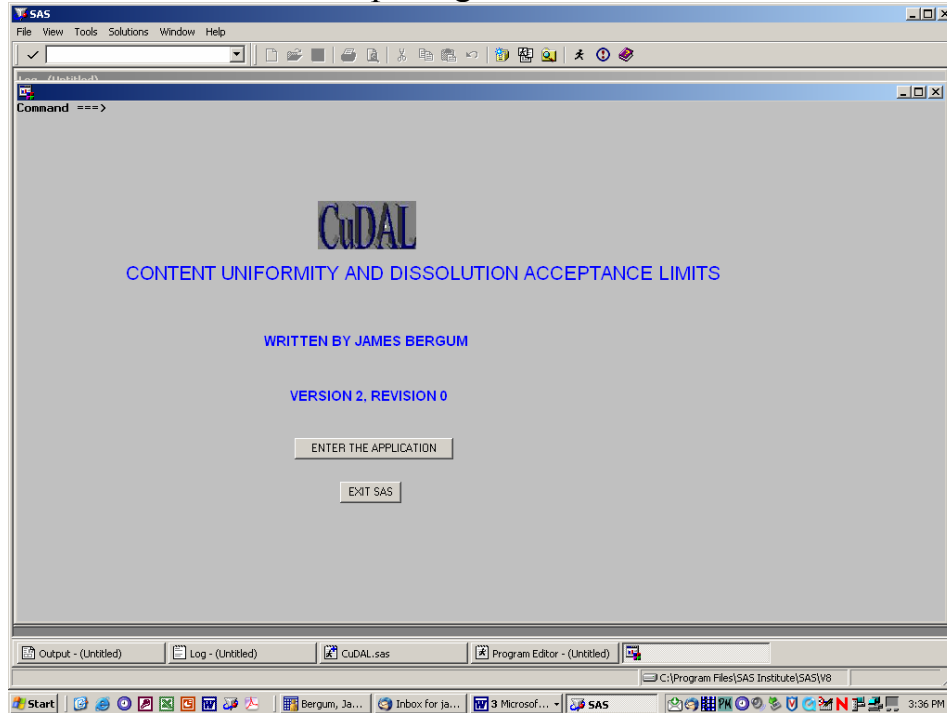
```
233.      %IF %UPCASE(&A2DISP2)=Y %THEN %DO;
234.      %EVDISP2;
235.      PROC DATASETS LIBRARY=WORK;
236.      DELETE SAVES2E;
237.      %END;
238.      %IF %UPCASE(&A3DISP2)=Y %THEN %DO;
239.      %SMPDISP2;
240.      %END;
241.      %MEND ANADISP2;

242.      %ANADISP2

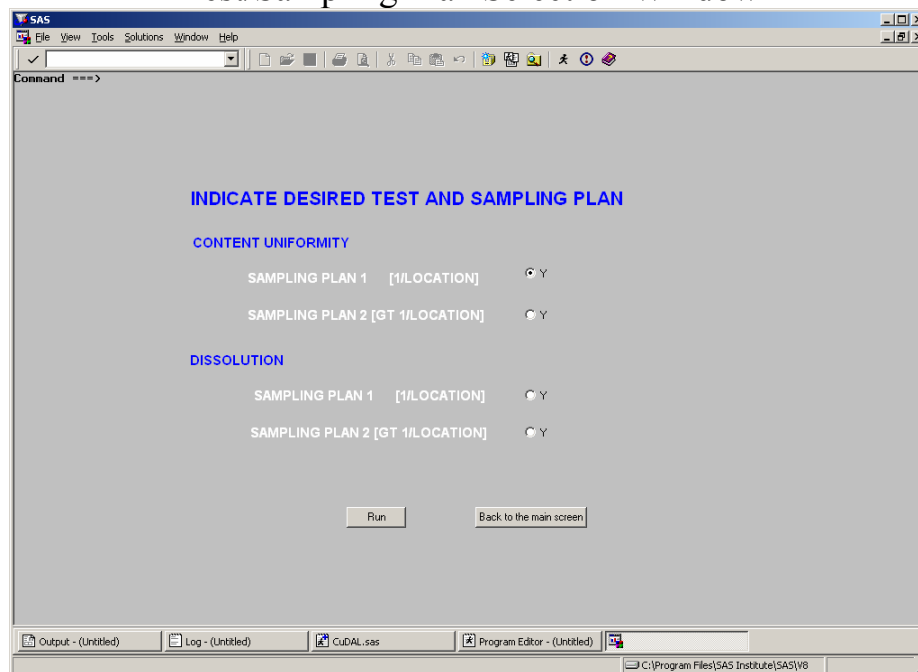
243.      RUN;
244.      %MEND DISP2;
245.      %DISP2
```

APPENDIX B WINDOWS

Opening Window:



Test/Sampling Plan Selection Window



Content Uniformity/Sampling Plan 1 Initial Window

SAS

File View Tools Solutions Window Help

Command ===> |

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

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

Run Cancel

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

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

Start | ... | 3:43 PM

Evaluation Sub-Window

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\V8

Start | ... | 3:44 PM

Lower Bound for Sample Result Sub-Window

This screenshot shows the 'Lower Bound for Sample Result Sub-Window' in SAS. The window has a title bar with 'SAS' and standard window controls. Below the title bar is a menu bar (File, View, Tools, Solutions, Window, Help) and a toolbar. The main area contains the following text and input fields:

TO DETERMINE LOWER BOUND FOR
FOUND SAMPLE RESULTS

ENTER SAMPLE MEAN (% CLAIM):

ENTER SAMPLE CV (%):

At the bottom are 'Run' and 'Cancel' buttons. The status bar at the very bottom shows the file path 'C:\Program Files\SAS Institute\SAS\V8' and the time '3:45 PM'.

Content Uniformity/Sampling Plan 2 Initial Screen

This screenshot shows the 'Content Uniformity/Sampling Plan 2 Initial Screen' in SAS. The window has a title bar with 'SAS' and standard window controls. Below the title bar is a menu bar (File, View, Tools, Solutions, Window, Help) and a toolbar. The main area contains the following text and input fields:

CONTENT UNIFORMITY ACCEPTANCE LIMIT PROGRAM FOR
SAMPLING PLAN 2 (GREATER THEN ONE SAMPLE PER LOCATION)

ENTER NUMBER OF LOCATIONS:

ENTER NUMBER PER LOCATION:

ENTER TARGET:

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 are 'Run' and 'Cancel' buttons. The status bar at the very bottom shows the file path 'C:\Program Files\SAS Institute\SAS\V8' and the time '3:46 PM'.

Evaluation Sub-Window

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 [Taskbar icons] 3:47 PM

Lower Bound for Sample Result Sub-Window

Command ==>

TO DETERMINE LOWER BOUND FOR FOUND SAMPLE RESULTS

ENTER SAMPLE MEAN (% CLAIM): 100

ENTER SAMPLE WITHIN STD DEV (% CLAIM): 2.2

ENTER SAMPLE BETWEEN STD DEV (% CLAIM): 2.46

(I.E. STANDARD DEVIATION OF SAMPLE LOCATION MEANS)

Run Cancel

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

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

Start [Taskbar icons] 3:47 PM

Dissolution/Sampling Plan 1 Initial Window

Command ==>

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

ENTER Q VALUE: 80

ENTER SAMPLE SIZE: 6

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\V8

Start | [Icons] | Bergum, Ja... | Inbox for ja... | 3 Microsoft... | SAS | [Icons] | 3:49 PM

Evaluation Window

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\V8

Start | [Icons] | Bergum, Ja... | Inbox for ja... | 3 Microsoft... | SAS | [Icons] | 3:49 PM

Lower Bound for Sample Result Sub-Window

Command ==> |

TO DETERMINE LOWER BOUND FOR FOUND SAMPLE RESULTS

ENTER SAMPLE MEAN (% CLAIM): 100

ENTER SAMPLE CV (%): 4

Run Cancel

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

C:\Program Files\SAS Institute\SAS\V8 3:49 PM

Dissolution/Sampling Plan 2 Initial Window

Command ==> |

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

ENTER O: 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\V8 3:50 PM

Evaluation Sub-Window

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\V8

Start [Taskbar Icons] 3:50 PM

Lower Bound for Sample Result Sub-Window

Command ==>

TO DETERMINE LOWER BOUND FOR FOUND SAMPLE RESULTS

ENTER SAMPLE MEAN (% CLAIM): 100

ENTER SAMPLE WITHIN STD DEV (% CLAIM): 2.2

ENTER SAMPLE BETWEEN STD DEV (% CLAIM): 2.46

(I.E. STANDARD DEVIATION OF SAMPLE LOCATION MEANS)

Run Cancel

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

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

Start [Taskbar Icons] 3:50 PM

APPENDIX C

DEFAULT WINDOW OUTPUT

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	2.74	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	4.02	105.6	2.63	110.6	1.36
85.7	0.65	90.7	2.02	95.7	3.25	100.7	3.99	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	3.82	106.3	2.44	111.3	1.19
86.4	0.85	91.4	2.20	96.4	3.41	101.4	3.79	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	3.62	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	3.48	107.5	2.13	112.5	0.90
87.6	1.19	92.6	2.50	97.6	3.68	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	3.34	108.0	2.00	113.0	0.79
88.1	1.33	93.1	2.63	98.1	3.79	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	3.92	103.7	3.14	108.7	1.83	113.7	0.63
88.8	1.52	93.8	2.80	98.8	3.94	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	3.01	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	4.09	104.5	2.92	109.5	1.63	114.5	0.44
89.6	1.73	94.6	2.99	99.6	4.11	104.6	2.90	109.6	1.60	114.6	0.42
89.7	1.76	94.7	3.01	99.7	4.13	104.7	2.87	109.7	1.58	114.7	0.40
89.8	1.79	94.8	3.04	99.8	4.15	104.8	2.84	109.8	1.55	114.8	0.38
89.9	1.81	94.9	3.06	99.9	4.17	104.9	2.82	109.9	1.53	114.9	0.35
90.0	1.84	95.0	3.08	100.0	4.19	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

		PROBABILITY OF PASSING
U	CV	
95	1	1.00000
100	1	1.00000
95	4	0.05235
100	4	0.56653

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	0.98041

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

92.9	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
93.0	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
93.1	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
93.2	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
93.3	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
93.4	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
93.5	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
93.6	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
93.7	94.4	105.6	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																		
SE	0.1		0.2		0.3		0.4		0.5		0.6		0.7		0.8		0.9	
	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	96.2	103.8	96.4	103.6	96.6	103.4
4.1	95.6	104.4	95.8	104.2	95.9	104.1	96.0	104.0	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	96.0	104.0	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	96.3	103.7	96.5	103.5	96.6	103.4	96.8	103.2	96.9	103.1	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	98.3	101.7
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	98.6	101.4
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	98.9	101.1
4.9	98.0	102.0	98.1	101.9	98.3	101.7	98.4	101.6	98.6	101.4	98.7	101.3	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	99.2	100.8	99.4	100.6	99.6	100.4
5.1	98.7	101.3	98.8	101.2	99.0	101.0	99.1	100.9	99.3	100.7	99.5	100.5	99.6	100.4	99.8	100.2	100.0	100.0
5.2	99.2	100.8	99.3	100.7	99.5	100.5	99.6	100.4	99.8	100.2	100.0	100.0						

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	95.0	105.0	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	95.9	104.1	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

STANDARD DEVIATIONS AND MEANS ARE EXPRESSED IN % CLAIM

[illegible]

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																		
1.9			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	97.6	102.4	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	98.8	101.2	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	99.4	100.6
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	99.5	100.5
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	98.4	101.6	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	99.7	100.3
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	97.6	102.4	98.2	101.8	98.8	101.2	99.3	100.7	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	98.4	101.6	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	98.9	101.1	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	97.4	102.6	97.9	102.1	98.4	101.6	98.9	101.1	99.4	100.6	99.9	100.1				

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	98.2	101.8	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	99.0	101.0	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	99.8	100.2		
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	99.9	100.1				

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	0.09184
2	100	2.2	2.2	0.56046

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	0.98769

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

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

J

(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)

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

[illegible]

12.25

12.50

12.75

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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

13.00

13.25

13.50

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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 (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 D NAVIGATION & ERROR CHECKS

Navigation (See Appendix B for window displays and names):

Test	Window	Instruction	Expected Result	Found Result	Agree (Y or N)
1	Opening Window	'Exit SAS'	Exit's SAS		
2	Opening Window	'Enter the Application'	Opens Test/Sampling Plan Selection Window		
	Test/Sampling Plan Selection Window	Select Content Uniformity - Sampling Plan 1	Opens Initial Content Uniformity Sampling Plan 1 Window		
	Initial Content Uniformity Sampling Plan 1 Window	Select 'Cancel'	Returns to Test/Sampling Plan Selection Window		
	Test/Sampling Plan Selection Window	Select Content Uniformity - Sampling Plan 1	Opens Initial Content Uniformity Sampling Plan 1 Window		
	Initial Content Uniformity Sampling Plan 1 Window	Select Yes to Print Table, Evaluate Table, and Find Lower Bound for a sample result. Select 'Run'	Opens Evaluation Sub-Window		
	Evaluation Sub-Window	Select 'Run'	Opens Lower Bound for Sample Result Sub-Window		
	Sample Result Sub-Window	Select 'Run'	Returns to Initial Content Uniformity Sampling Plan 1 Window		
	Initial Content Uniformity Sampling Plan 1 Window	Select 'Cancel'	Returns to Test/Sampling Plan Selection Window		
	Test/Sampling Plan Selection Window	Select 'Cancel'	Returns to Opening Window		
3	Opening Window	Select 'Enter the Application', Select Content Uniformity - Sampling Plan 2	Opens Initial Content Uniformity Sampling Plan 2 Window		
	Initial Content Uniformity Sampling Plan 2 Window	Select 'Cancel'	Returns to Test/Sampling Plan Selection Window		
	Test/Sampling Plan Selection Window	Select Content Uniformity - Sampling Plan 2	Opens Initial Content Uniformity Sampling Plan 2 Window		
	Initial Content Uniformity Sampling Plan 2 Window	Select Yes to Print Table, Evaluate Table, and Find Lower Bound for a sample result. Select 'Run'	Opens Evaluation Sub-Window		
	Evaluation Sub-Window	Select 'Run'	Opens Lower Bound for Sample Result Sub-Window		
	Sample Result Sub-Window	Select 'Run'	Returns to Initial Content Uniformity		

			Sampling Plan 2 Window		
	Initial Content Uniformity Sampling Plan 2 Window	Select 'Cancel'	Returns to Test/Sampling Plan Selection Window		
	Test/Sampling Plan Selection Window	Select 'Cancel'	Returns to Opening Window		
4	Opening Window	Select 'Enter the Application', Select Dissolution - Sampling Plan 1	Opens Initial Dissolution - Sampling Plan 1 Window		
	Initial Dissolution Sampling Plan 1 Window	Select 'Cancel'	Returns to Test/Sampling Plan Selection Window		
	Test/Sampling Plan Selection Window	Select Dissolution - Sampling Plan 1	Opens Initial Dissolution Sampling Plan 1 Window		
	Initial Dissolution Sampling Plan 1 Window	Select Yes to Print Table, Evaluate Table, and Find Lower Bound for a sample result. Select 'Run'	Opens Evaluation Sub-Window		
	Evaluation Sub-Window	Select 'Run'	Opens Lower Bound for Sample Result Sub-Window		
	Sample Result Sub-Window	Select 'Run'	Returns to Initial Dissolution Sampling Plan 1 Window		
	Initial Dissolution Sampling Plan 1 Window	Select 'Cancel'	Returns to Test/Sampling Plan Selection Window		
	Test/Sampling Plan Selection Window	Select 'Cancel'	Returns to Opening Window		
5	Opening Window	Select 'Enter the Application', Select Dissolution - Sampling Plan 2	Opens Initial Dissolution Sampling Plan 2 Window		
	Initial Dissolution Sampling Plan 2 Window	Select 'Cancel'	Returns to Test/Sampling Plan Selection Window		
	Test/Sampling Plan Selection Window	Select Dissolution - Sampling Plan 2	Opens Initial Dissolution Sampling Plan 2 Window		
	Initial Dissolution Sampling Plan 2 Window	Select Yes to Print Table, Evaluate Table, and Find Lower Bound for a sample result. Select 'Run'	Opens Evaluation Sub-Window		
	Evaluation Sub-Window	Select 'Run'	Opens Lower Bound for Sample Result Sub-Window		
	Sample Result Sub-Window	Select 'Run'	Returns to Initial Dissolution Sampling Plan 2 Window		
	Initial Dissolution Sampling Plan 1 Window	Select 'Cancel'	Returns to Test/Sampling Plan Selection Window		
	Test/Sampling Plan Selection Window	Select 'Cancel'	Returns to Opening Window		

**APPENDIX D
WINDOW INPUT ERROR CHECKING
TEST DATA**

**CONTENT UNIFORMITY
SAMPLING PLAN 1**

Window	Requested Input	User Input	EXPECTED RESPONSE	FOUND RESPONSE	AGREE? (Y or N)
			N = NONE	N or ES	
			ES = ERROR SCREEN		
Initial Window	Sample Size	5	N		
		4	ES		
		2000	N		
	Bound	50	N		
		99	N		
		49.9	ES		
		99.1	ES		
		75	N		
	Confidence Interval	50	N		
		99	N		
		49.9	ES		
		99.1	ES		
		65	N		
Evaluate Sub Window	Lower Bound Mean	0	ES		
	Upper Bound Mean	0	ES		
	Increment Mean	0	ES		
	Lower Bound CV	0	ES		
	Upper Bound CV	0	ES		
	Increment CV	0	ES		
Lower Bound Based on Sample Result	Sample Mean	85.1	N		
		114.9	N		
		85	ES		
		115	ES		
		100.123	N		
	Sample CV	0.1	N		
		0	ES		
		15	N		
		-3	ES		

**CONTENT UNIFORMITY
SAMPLING PLAN 2**

Window	Requested Input	User Input	EXPECTED RESPONSE	FOUND RESPONSE	AGREE? (Y or N)
			N = NONE	N or ES	
			ES = ERROR SCREEN		
Initial Window	Number of Locations	3	N		
		2	ES		
		2000	N		
	Number per location	2	N		
		1	ES		
		2000	N		
	Bound	50	N		
		99	N		
		49.9	ES		
		99.1	ES		
		80	N		
	Confidence Level	50	N		
		99	N		
		49.9	ES		
		99.1	ES		
		70	N		
Evaluate Sub-Window	Lower Bound Mean	0	ES		
	Upper Bound Mean	0	ES		
	Increment Mean	0	ES		
	Lower Bound Within SD	0	ES		
	Upper Bound Within SD	0	ES		
	Increment Within SD	0	ES		
	Lower Bound Between SD	0	ES		
	Upper Bound Between SD	0	ES		
	Increment Between SD	0	ES		
Lower Bound Based on Sample Result	Sample Mean	85.1	N		
		114.9	N		
		85	ES		
		115	ES		
		100.123	N		
	Sample Within SD	0.1	N		
		0	ES		
		15	N		
		-3	ES		
	Sample Between SD	0.1	N		
		0	ES		
		15	N		
		-3	ES		

**DISSOLUTION
SAMPLING PLAN 1**

Window	Requested Input	User Input	EXPECTED RESPONSE	FOUND RESPONSE	AGREE? (Y or N)
			N = NONE	N or ES	
			ES = ERROR SCREEN		
Initial Window	Q	40	N		
		95	N		
		39.9	ES		
		95.1	ES		
	Sample Size	3	N		
		2	ES		
		2000	N		
	Bound	50	N		
		99	N		
		49.9	ES		
		99.1	ES		
		75	N		
	Confidence Level	50	N		
		99	N		
		49.9	ES		
		99.1	ES		
		80	N		
Evaluate Sub Window	Lower Bound Mean	0	ES		
	Upper Bound Mean	0	ES		
	Increment Mean	0	ES		
	Lower Bound CV	0	ES		
	Upper Bound CV	0	ES		
	Increment CV	0	ES		
Lower Bound Based on Sample Result	Sample Mean	75.1	N		
	(Q = 75)	100	N		
		85.5	N		
		75	ES		
	Sample CV	0.1	N		
		0	ES		
		15	N		
		-3	ES		

**DISSOLUTION
SAMPLING PLAN 2**

Window	Requested Input	User Input	EXPECTED RESPONSE	FOUND RESPONSE	AGREE? (Y or N)
			N = NONE	N or ES	
			ES = ERROR SCREEN		
Initial Window	Q	40	N		
		95	N		
		39.9	ES		
		95.1	ES		
	Number of Locations	3	N		
		2	ES		
		2000	N		
	Number per Location	2	N		
		1	ES		
		2000	N		
	Bound	50	N		
		99	N		
		49.9	ES		
		99.1	ES		
		65	N		
	Confidence Level	50	N		
		99	N		
		49.9	ES		
		99.1	ES		
		80	N		
Evaluate Sub-Window	Lower Bound Mean	0	ES		
	Upper Bound Mean	0	ES		
	Increment Mean	0	ES		
	Lower Bound Within SD	0	ES		
	Upper Bound Within SD	0	ES		
	Increment Within SD	0	ES		
	Lower Bound Between SD	0	ES		
	Upper Bound Between SD	0	ES		
	Increment Between SD	0	ES		
Lower Bound Based on Sample Result	Sample Mean	60.1	N		
	(Q = 60)	100	N		
		80.6	N		
		60	ES		
	Sample Within SD	0.1	N		
		0	ES		
		15	N		
		-3	ES		
	Sample Between SD	0.1	N		
		0	ES		
		15	N		
		-3	ES		

APPENDIX E LOWER BOUND CALCULATIONS

The calculations used for Content Uniformity are described below:

The revised content uniformity test is a two stage test. The uniformity of dosage units for the revised test can be demonstrated by either of two methods - Content Uniformity or Weight Variation. The derivations that follow are based on the individual dosage values obtained by either of the two methods. Let S_i be the criteria of passing stage i , $i=1,2$. To meet the content uniformity test, test 10 dosage units and the requirements are met if S_1 is satisfied. Otherwise, test the next 20 units. The requirements are met if S_2 is satisfied. Let $L_1 = 15$ and $L_2 = 25$. The criteria of S_1 and S_2 are as follows:

S_1 = The acceptance value (defined below) of the first 10 dosage units is $\leq L_1$

- S_2 = i) The acceptance value of the 30 dosage units is $\leq L_1$
- ii) No dosage unit is outside the maximum allowed range, L_2 , which is the deviation of each dosage unit tested from the calculated value of M (defined below).

T 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. We now define M as follows:

When $T \leq 101.5$

$$\begin{aligned} \text{Then } M &= \max\{98.5, \bar{X}\} \quad \text{if } \bar{X} \leq 100 \\ M &= \min\{101.5, \bar{X}\} \quad \text{if } \bar{X} > 100 \end{aligned}$$

When $T > 101.5$

$$\begin{aligned} \text{Then } M &= \max\{98.5, \bar{X}\} \quad \text{if } \bar{X} \leq 100 \\ M &= \min\{T, \bar{X}\} \quad \text{if } \bar{X} > 100 \end{aligned}$$

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

Where $k = 2.4$ for $n=10$; $k = 2.0$ for $n=30$

s is the standard deviation of the observations.

Unless otherwise specified, all the measurements of dosage units and criteria values (such as L_1 and L_2) are in percentage label claim.

Lower Probability Bound of Passing USP

Notice that

$$\begin{aligned} P(\text{passing ICH test}) &= P(S_1 \text{ or } (\bar{S}_1 \text{ and } S_2)) \\ &= P(S_1) + P(\bar{S}_1 \text{ and } S_2) - P(S_1 \text{ and } (\bar{S}_1 \text{ and } S_2)) \\ &= P(S_1) + P(\bar{S}_1 \text{ and } S_2), \end{aligned}$$

where P denotes probability and \bar{S}_1 denotes failing S_1 .

Using the fact that $P(S_1) + P(\bar{S}_1 \text{ and } S_2) \geq P(S_1)$

and $P(S_1) + P(\bar{S}_1 \text{ and } S_2) \geq P(S_1 \text{ and } S_2) + P(\bar{S}_1 \text{ and } S_2) = P(S_2)$

we have $P(\text{passing ICH test}) \geq \max\{P(S_1), P(S_2)\}$.

Denote the sample measurements of dosage units as $X_i, i=1, \dots, n$. Assume that the X_i 's follow a normal distribution with $N(\mu, \sigma)$. Then the values of $P(S_1)$ and $P(S_2)$ can be calculated as described in the following two subsections.

Computation of $P(S_1)$. Due to the definition of acceptance value, it can be seen that

For $T \leq 101.5$

$$\text{Acceptance Value} = \begin{cases} 98.5 - \bar{X} + ks & \text{if } \bar{X} < 98.5 \\ ks & \text{if } 98.5 \leq \bar{X} \leq 101.5 \\ \bar{X} - 101.5 + ks & \text{if } \bar{X} > 101.5 \end{cases}$$

For $T > 101.5$

$$\text{Acceptance Value} = \begin{cases} 98.5 - \bar{X} + ks & \text{if } \bar{X} < 98.5 \\ ks & \text{if } 98.5 \leq \bar{X} \leq T \\ \bar{X} - T + ks & \text{if } \bar{X} > T \end{cases}$$

For $T \leq 101.5$,

$$\begin{aligned} P(S_1) = & P(98.5 \leq \bar{X} \leq 101.5 \text{ and } k_1 s < L_1) \\ & + P(\bar{X} > 101.5 \text{ and } \bar{X} - 101.5 + k_1 s < L_1) \\ & + P(\bar{X} < 98.5 \text{ and } 98.5 - \bar{X} + k_1 s < L_1), \end{aligned}$$

where $k_1 = 2.4$.

By the central Limit Theorem, $\bar{X} = \frac{1}{n} \sum_{i=1}^n X_i$ follows a normal distribution with mean μ and standard deviation σ / \sqrt{n} denoted as $N(\mu, \sigma / \sqrt{n})$. Also $(n-1)s^2/\sigma^2$ follows a χ^2 distribution with $n-1$ degrees of freedom where

$$\text{standard deviation } s = \sqrt{\frac{1}{n-1} \sum_{i=1}^n (X_i - \bar{X})^2}$$

\bar{X} and S^2 are independent variables. The joint density of (\bar{X}, s^2) can be calculated by the product of their densities.

Denote $Z_1 = \bar{X}$ and $Z_2 = (n-1)s^2/\sigma^2$.

The density functions $f(Z_1)$ and $f(Z_2)$ are

$$f(Z_1 = z_1) = \frac{1}{\sigma \sqrt{2\pi}} e^{-\frac{(z_1 - \mu)^2}{2\sigma^2}}$$

$$f(Z_2 = z_2) = \frac{1}{\Gamma(r/2) 2^{r/2}} z_2^{r/2-1} e^{-z_2/2} \quad \text{for } z_2 \geq 0.$$

where $\gamma = n-1$ and $\Gamma(p) = \int_0^\infty t^{p-1} e^{-t} dt$.

The density function of Z_2 is a Chi-Square distribution with $n-1$ degrees of freedom and is denoted as $\chi^2_{(n-1)}$.

The joint density function is $f(z_1, z_2) = f(z_1) f(z_2)$,

Due to the independency of Z_1 and Z_2 , $P(S_1)$ in terms of Z_1 and Z_2 , can be rewritten as

$$P(S_1) = P(98.5 \leq Z_1 \leq 101.5 \text{ and } k_1 \sigma \sqrt{\frac{Z_2}{(n-1)}} < L_1)$$

$$\begin{aligned}
& + P(Z_1 > 101.5 \text{ and } Z_1 - 101.5 + k_1 \sigma \sqrt{\frac{Z_2}{(n-1)}} < L_1) \\
& + P(Z_1 < 98.5 \text{ and } 98.5 - Z_1 + k_1 \sigma \sqrt{\frac{Z_2}{(n-1)}} < L_1) \\
& = I_1 + I_2 + I_3,
\end{aligned}$$

where

$$\begin{aligned}
I_1 &= P(98.5 \leq Z_1 \leq 101.5 \text{ and } k_1 \sigma \sqrt{\frac{Z_2}{(n-1)}} < L_1) \\
I_2 &= P(Z_1 > 101.5 \text{ and } Z_1 - 101.5 + k_1 \sigma \sqrt{\frac{Z_2}{(n-1)}} < L_1) \\
I_3 &= P(Z_1 < 98.5 \text{ and } 98.5 - Z_1 + k_1 \sigma \sqrt{\frac{Z_2}{(n-1)}} < L_1)
\end{aligned}$$

Notice that

$$\begin{aligned}
I_1 &= P(98.5 \leq Z_1 \leq 101.5) * P(k_1 \sigma \sqrt{\frac{Z_2}{(n-1)}} < L_1) \\
&= (\Phi(t_1) - \Phi(t_2)) * P(Z_2 < (n-1) * L_1^2 / (k_1^2 \sigma^2))
\end{aligned}$$

with $t_1 = \sqrt{n}(101.5 - \mu) / \sigma$ and $t_2 = \sqrt{n}(98.5 - \mu) / \sigma$

and Φ the cumulative density function of standard normal $N(0,1)$.

Let $g(z_1) = (n-1)(L_1 + 101.5 - z_1)^2 / (k_1 \sigma)^2$. Noting that that $L_1 = 15$, we have

$$\begin{aligned}
I_2 &= P(Z_1 > 101.5 \text{ and } Z_2 < g(Z_1)) \\
&= \int_{101.5}^{101.5+15} f(z_1) \int_0^{g(z_1)} f(z_2) dz_2 dz_1
\end{aligned} \tag{1}$$

Let $h(z_1) = (n-1)(L_1 - 98.5 + z_1)^2 / (k_1 \sigma)^2$. Then

$$I_3 = P(Z_1 < 98.5 \text{ and } Z_2 < h(Z_1))$$

$$= \int_{98.5-15}^{98.5} f(z_1) \int_0^{h(z_1)} f(z_2) dz_2 dz_1 \quad (2)$$

The integrations of (1) and (2) have no analytical results due to the complexities of their integrands. However, numerical results of the integrations can be calculated. For a Chi-Square distribution with k degrees of freedom, the function PROBCHI(y,k) in SAS provides the numerical result of integration $\int_0^y f(z_2) dz_2$ for given y. Taking advantage of known function PROBCHI(y,k), the numerical integrations of (1) and (2) are calculated as follows:

$$I_2 = \lim_{h \rightarrow 0} \sum_{i=1}^K (\Phi(Z_1 + ih) - \Phi(Z_1 + (i-1)h)) \text{PROBCHI}(g(Z_1 + (i-1/2)h), n-1)$$

where $K = \lceil L_1/h \rceil$, the number of intervals of width h. Similarly, for I_3 ,

$$I_3 = \lim_{h \rightarrow 0} \sum_{i=1}^K (\Phi(Z_1 + ih) - \Phi(Z_1 + (i-1)h)) \text{PROBCHI}(h(Z_1 + (i-1/2)h), n-1)$$

A small program in SAS can be programmed to carry out the calculation. Therefore, $P(S_1)$ can be calculated as

$$P(S_1) = (\Phi(t_1) - \Phi(t_2)) * P(Z_2 < (n-1) * L_1^2 / (k^2 \sigma^2)) + I_2 + I_3$$

A similar calculation can be performed for $T > 101.5$ by replacing 101.5 in the above equations with T.

Computation of $P(S_2)$ There are two sub-criteria in S_2 which are denoted as C_{21} and C_{22} respectively as follows:

C_{21} = AV of the 30 dosage units is less than or equal to L_1 .

C_{22} = No unit is over the deviation of L_2 from the calculated value of M.

Using the inequality that, for two events A and B,

$$P(A \text{ and } B) = P(A) + P(B) - P(A \text{ or } B) \geq P(A) + P(B) - 1.$$

One gets $P(S_2) = P(C_{21} \text{ and } C_{22}) \geq \max\{P(C_{21}) + P(C_{22}) - 1, 0\}$

Since criteria C_{21} is very similar to S_1 except for $n=30$ and $k=2.0$ in the former while $n=10$ and $k=2.4$ in the later, the calculation of $P(C_{21})$ is carried out similarly as in $P(S_1)$ with $n=30$ and $k=2.0$. Therefore,

$$P(C_{21}) = (\Phi(t_1) - \Phi(t_2)) * P(Z_2 < (n-1) * L_1^2 / (k^2 \sigma^2))$$

$$\begin{aligned}
& + \lim_{h \rightarrow 0} \sum_{i=1}^K (f(z_1 + ih) - f(z_1 + (i-1)h)) \text{PROBCHI}(g(z_1 + (i-1/2)h), n-1) \\
& + \lim_{h \rightarrow 0} \sum_{i=1}^K (f(z_1 + ih) - f(z_1 + (i-1)h)) \text{PROBCHI}(h(z_1 + (i-1/2)h), n-1)
\end{aligned}$$

where $n = 30$ and $k_2 = 2.0$. For the calculation of $P(C_{22})$, notice that

For $T \leq 101.5$

$$M = \begin{cases} 98.5 & \text{if } \bar{X} < 98.5 \\ \bar{X} & \text{if } 98.5 \leq \bar{X} \leq 101.5 \\ 101.5 & \text{if } \bar{X} > 101.5 \end{cases}$$

Then, with $L_2 = 25$,

$$\begin{aligned}
P(C_{22}) &= P(98.5 \leq \bar{X} \leq 101.5 \text{ and } |X_i - \bar{X}| < L_2, i = 1, \dots, n) \\
&+ P(\bar{X} > 101.5 \text{ and } |X_i - 101.5| < L_2, i = 1, \dots, n) \\
&+ P(\bar{X} < 98.5 \text{ and } |X_i - 98.5| < L_2, i = 1, \dots, n) \\
&= P(98.5 \leq \bar{X} \leq 101.5 \text{ and } \bar{X} - L_2 < X_i < \bar{X} + L_2, i = 1, \dots, n) \\
&+ P(\bar{X} > 101.5 \text{ and } 101.5 - L_2 < X_i < 101.5 + L_2, i = 1, \dots, n) \\
&+ P(\bar{X} < 98.5 \text{ and } 98.5 - L_2 < X_i < 98.5 + L_2, i = 1, \dots, n) \\
&\geq P(101.5 - L_2 < X_i < 98.5 + L_2, i = 1, \dots, n) \\
&= [\Phi((98.5 + L_2 - \mu) / (\sigma / \sqrt{n})) - \Phi((101.5 - L_2 - \mu) / (\sigma / \sqrt{n}))]^n
\end{aligned}$$

For $T > 101.5$

$$M = \begin{cases} 98.5 & \text{if } \bar{X} < 98.5 \\ \bar{X} & \text{if } 98.5 \leq \bar{X} \leq T \\ T & \text{if } \bar{X} > T \end{cases}$$

Then, with $L_2 = 25$,

$$\begin{aligned} P(C_{22}) &= P(98.5 \leq \bar{X} \leq T \quad \text{and } |X_i - \bar{X}| < L_2, i = 1, \dots, n) \\ &\quad + P(\bar{X} > T \quad \text{and } |X_i - T| < L_2, i = 1, \dots, n) \\ &\quad + P(\bar{X} < 98.5 \quad \text{and } |X_i - 98.5| < L_2, i = 1, \dots, n) \\ &= P(98.5 \leq \bar{X} \leq T \quad \text{and } \bar{X} - L_2 < X_i < \bar{X} + L_2, i = 1, \dots, n) \\ &\quad + P(\bar{X} > T \quad \text{and } T - L_2 < X_i < T + L_2, i = 1, \dots, n) \\ &\quad + P(\bar{X} < 98.5 \quad \text{and } 98.5 - L_2 < X_i < 98.5 + L_2, i = 1, \dots, n) \\ &\geq P(T - L_2 < X_i < 98.5 + L_2, i = 1, \dots, n) \\ &= [\Phi((98.5 + L_2 - \mu)/\sigma) - \Phi((T - L_2 - \mu)/\sigma)]^n \end{aligned}$$

A lower bound of the probability of passing ICH requirements is $P(\text{Passing ICH}) \geq \max\{P(S_1), P(S_2)\}$

The USP dissolution test and calculations are as follows:

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

Pass if the following criteria are met:

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

Calculation:

$P(\text{meeting criteria of stage 1})$

$$= [P(x \geq Q + 5)]^6$$

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 $\leq Q - 15$

Calculation:

$P(\text{passing 1}^{\text{st}} \text{ criteria of stage 2})$

$$= P(\text{Mean} \geq Q)$$

$P(\text{passing 2}^{\text{nd}} \text{ criteria of stage 2})$

$$= [P(x \geq Q - 15)]^{12}$$

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 $\leq Q - 25$

Calculation:

$P(\text{passing 1}^{\text{st}} \text{ criteria of stage 3})$

$$= P(\text{Mean result} \geq Q)$$

$P(\text{passing 2}^{\text{nd}} \text{ criteria of stage 3})$

$$= [P(x \geq Q - 15)]^{24} + 24 [P(Q - 25 \leq x \leq Q - 15)] [P(x \geq Q - 15)]^{23} + 276 [P(Q - 25 \leq x \leq Q - 15)]^2 [P(x \geq Q - 15)]^{22}$$

APPENDIX F PROGRAM DESCRIPTION

Each of the five programs (excludes programs for GUI) included in CuDAL are described below. Macros are italicized. To aid in locating the macro's and windows in the SAS™ programs, brackets enclose the associated program line numbers.

PROGRAM: CuDAL.SAS - Used to define file locations

The file CuDAL.SAS shown below provides the location of the four analysis macro's (CUSP1.SAS, CUSP2.SAS, DISP1.SAS, and DISP2.SAS) and the two files for the GUI interface/navigation (cudal.sas7bcat and Files.sas.org). In each of these lines of code, the user replaces D:\V2 with the appropriate directory locations. This is the only file that requires editing.

```
***** 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('%syndel ' || trim(left(name)) || ';' );  
run;  
  
libname cudal 'D:\V2';  
options symbolgen mprint mlogic sasautos=('D:\V2');  
  
dm 'af c=cudal.cudal.welcome.frame; ' continue;
```

PROGRAM: CUSP1.SAS - Used to generate Content Uniformity acceptance limits using Sampling Plan 1

The macros contained in CUSP1.SAS are described below:

clcalc [52-162]-

This macro is used to calculate the lower bound on passing the USP content uniformity test given a pair of specific values for μ and σ . The macro *calculuspl* passes two points in the confidence region for μ and σ to evaluate. Both of these points have the largest value of σ (SIGMA) in the confidence region. One point has the smallest value of μ (LLU) and the other the largest value for μ (ULU). The pair LLU, SIGMA is evaluated first, then the pair ULU, SIGMA. PROBNORM is used to calculate the probability of meeting the CV criteria and

to calculate the normal probability of an individual value falling within a given interval. Since the probability of passing the USP test is greater than or equal to the probability of passing any individual stage, the maximum probability of passing is selected from stage 1 (LPROB1) and stage 2 (LPROB2) for each point. Finally, the lowest probability of passing the USP test occurs with the pair with the lowest probability of passing so the minimum probability (OVERBD) is selected from the two evaluated points.

*calcu*sp1[163-228]-

This macro determines the largest value for the sample CV such that for all points in the confidence region for μ and σ , the probability of passing the USP test for content uniformity is greater than the user specified lower bound (LBOUND). The confidence interval is a triangle. The only two points to evaluate on the triangle are the two points with the maximum value of sigma. So, for a given value of the sample mean, the strategy is to start with a very small value for the sample standard deviation and then construct the corresponding confidence region for μ and σ . Then evaluate the two points corresponding to the largest value of σ and the smallest and largest values for μ . If both of the points result in probabilities greater than LBOUND, this means that all of the points in the entire confidence region would give a probability of passing the USP content uniformity test greater than LBOUND. Therefore, given the same sample mean, a larger value of the standard deviation can be evaluated. The value of the sample standard deviation is increased until one of the two points evaluated in the confidence region is less than LBOUND. The last value of the standard deviation is kept for the acceptance limit table. At a value of the sample mean around 100, the sample standard deviation will reach its maximum acceptance limit table value. The next sample mean evaluated after this maximum has been reached will have a lower value of the sample standard deviation. The program checks to determine when this occurs. At this point, the program starts generating the rest of the acceptance limit table by setting the sample mean to 114.9, resetting the sample standard deviation to a small value and works its way down from 114.9 to the value of the sample mean with the largest sample standard deviation.

The strategy described above is performed by using a DO loop that starts with a sample mean of 85.1 and increases to 114.9 in increments of 0.1 (set by macro variable D). The standard deviation starts at 0.01 (STARTSD) and increments by 0.001. For each value of the standard deviation (SAMPD), the upper bound for sigma (SIGMA) is calculated using the usual χ^2 based confidence bound formula. The two points in the confidence interval that will be evaluated are determined (LLU and ULU). LLU and ULU are the lower and upper ends of the confidence region associated with SIGMA. Since the sample mean and sample variance are independent, the overall α level (1- confidence level) is the product of the two individual α levels for μ and σ . So the two individual confidence levels are the square root of the overall α . Then the portion of the overall α used to estimate μ is

divided equally to construct a 2-tailed test. Since the confidence interval for σ is one-sided, the portion of the overall α for σ is all put into one tail. The macro *c1calc* is called to calculate the lower bound on the probability of passing the USP test for LLU and ULU. The minimum of the two probabilities (OVERBD) is returned from *c1calc*. If the minimum is greater than the lower bound selected by the user (LBOUND), the standard deviation (SAMPSTD) is incremented by 0.001 and a new LLU and ULU are computed and the minimum probability is found again. Once the minimum is less than the lower bound, 0.001 is subtracted from the standard deviation, and the CV is computed. A special case is when the starting value (STARTSD) of 0.01 gives a minimum less than the lower bound. In this case the CV is set to 0. The value of the standard deviation is used as a starting point for the next sample mean since the standard deviation must increase as the sample mean increases from 85.1 to around 100. At some value of the sample mean greater than 100, the standard deviation will start decreasing. In the macro, when a new sample mean is evaluated with the starting value of the previous standard deviation and the resulting OVERBD is less than the user pre-specified lower bound (LBOUND), this means that the maximum tabled sample standard deviation has been reached. Therefore, the macro saves the value of this mean (STARTM), goes to the label UPPER, sets the starting standard deviation back to 0.01, and starts a DO loop that starts with a sample mean (MEAN) at 114.9 and decreases by 0.1 to STARTM. The same procedure is used as described above to find the sample standard deviation for each sample mean.

Once the entire set of sample mean, CV combinations are determined, the data is sorted by MEAN and a data set is prepared for use in printing the table. This is done by creating six data sets. Each of these data sets contains the data for two columns of the printed acceptance table (one for the sample mean and one for the CV). Data set ONE contains the mean and CV for values of the sample mean between 85.1 and 90.0, data set TWO from 90.1 to 95.0, etc. All six of these data sets are then merged together to form data set SEVEN.

PRTCUSPI [229-241]-

This macro prints the acceptance limit table by printing out data set SEVEN prepared by the macro *calcuspl*.

EVCUSPI[242-272]-

This macro starts by defining a window (SMAIN [258-271]) for the user to specify the range of possible population values for the mean and CV. For the population mean, the user specifies the lower bound for the mean (ULOW), the upper bound for the mean (UHIGH), the increment (UINCRE), and the divisor (UDIV). Each of these values must be a positive integer. So if the user wants to evaluate population means from 98.0 to 102.0 by 0.5, the following values would be specified: ULOW = 980, UHIGH = 1020, UINCRE = 5, and UDIV = 10. The upper and lower values for the CV as well as the increment and divisor are input

in the same manner as those are for the mean. Finally, data set SEVEN is read into data set TAB. The macro DSCUSP1 [321-329] reads TAB and creates 6 data sets containing the sample means and standard deviations from TAB. The 6 data sets are appended to one another and stored in data set ONE.

The macro *SIGCUSP1* [337-362] performs the calculations for each population mean and CV combination. The strategy is as follows: The acceptance limit table consists of pairs of sample means with an upper bound on the sample CV. Data set ONE contains the sample mean and sample standard deviation pairs that make up the entire acceptance limit table. The table begins with a sample mean of 85.1 and ends with a sample mean of 114.9. To calculate the probability of passing the acceptance limit table for specified values for the population mean and population CV, the probability is calculated of a sample mean falling between adjacent means in the table and the sample standard deviation falling below the average standard deviation at the two endpoints. So, suppose the standard deviation at a sample mean of 85.1 was 0.2 and the sample standard deviation bound at a sample mean of 85.2 was 0.5. If the evaluation was at a population mean of 100 with standard deviation of 3, then the first calculation would be to find the probability of getting a sample mean between 85.1 and 85.2 and a sample standard deviation less than $(0.2 + 0.5)/2$ or 0.35. This is done using the SAS functions - PROBNORM and PROBCHI. The second calculation would calculate the probability of getting a sample means between 85.2 to 85.3 with a sample standard deviation less than the average of the corresponding standard deviations for 85.2 and 85.3. These probabilities are summed across all the intervals from 85.1 to 114.9. The sum of these probabilities (PTRAP) is the probability of passing the table for specific population values for the mean and standard deviation. To perform the calculation, the lag function in SAS is used to obtain the previous value for the sample mean and sample standard deviation. The last value of PTRAP is output. PROC APPEND is used to save the PTRAP value for each combination of CV and U in the DO loop. These values are stored in the data set SAVEALL. Finally, the data set SAVEALL is printed.

SMPCUSP1 [273-298]

This macro is used to calculate the lower bound of passing the USP content uniformity test given the sample mean and sample standard deviation. The data set TAB determines the endpoints of the confidence interval based on the user input values for the sample mean and standard deviation and prior information such as dosage form type, confidence level, and sample size. The overall α is divided into two portions as described above in the macro *calcusp1*. The macro *clcalc* is called to determine the lower bound. Finally, the lower bound is printed.

ANACUSP1 [299-315]

This macro is used to respond to the user input from the initial test/sampling plan window. If the user requests printing of the acceptance limit table or evaluation

of a table, then the macro *calcuspl* is called. If the user requests a printout of the acceptance limit table, the macro *PRTCUSPI* is called. If an evaluation is requested, the macro *EVCUSPI* is called. After the evaluation macro is finished the dataset SAVEALL is deleted. Finally, if the user requests a lower bound for a sample mean and standard deviation, the macro *SMPCUSPI* is called.

PROGRAM: CUSP2.SAS - Content Uniformity using Sampling Plan 2

The macros contained in CUSP2.SAS are defined below:

Cullu [62-119]

This macro performs the lower probability bound calculation for the point in the confidence region with the smallest value of μ (LLU) and largest value of σ (SIGMA). The calculation is performed as in *clcalc* using the SAS function PROBNORM. Since the probability of passing the USP test is greater than or equal to the probability of passing any individual stage, the maximum probability of passing is selected from stage 1 (LPROB1) and stage 2 (TPROBL2).

Cuulu [120-177]

This macro performs the lower probability bound calculation for the point in the confidence region with the largest value of μ (ULU) and largest value of σ (SIGMA). The calculation is performed as in *clcalc* using the SAS function PROBNORM. Since the probability of passing the USP test is greater than or equal to the probability of passing any individual stage, the maximum probability of passing is selected from stage 1 (LPROB1) and stage 2 (TPROBL2).

calcusp2 [178-258]

This macro finds the acceptance limit on the CV for a given mean. The confidence interval is a triangle. The only two points to evaluate on the triangle are the two points with the maximum value of sigma. However, the value of sigma is a function of both the between and within variance components. A method to construct a confidence interval for the sum of the within and between variance components is given in Graybill, F.A. & Wang, C., "Confidence Intervals on Nonnegative Linear Combinations of Variances", Journal of the American Statistical Association, December 1980, Volume 75, Number 372, p. 869 - 873.

Let

MS_L = Mean Square Between Locations from One-Way ANOVA

MS_E = Mean Square Within Locations from One-Way ANOVA

L = Number of Locations

n = Number observations at each location

Then the upper confidence limit for the sum of the between location and within location variance components (i.e. σ) is

$$\left[\frac{1}{n} MS_L + (1 - \frac{1}{n}) MS_E \right] + \left\{ \left[\frac{1}{n} ((L - 1) / \chi^2_{L-1} - 1) MS_L \right]^2 + \left[((1 - \frac{1}{n}) L (n - 1) / \chi^2_{L(n-1)} - 1) MS_E \right]^2 \right\}^{1/2}$$

The strategy is as follows: Given the sample within location standard deviation (SE) and the sample between location standard deviation (SM), a confidence interval for σ (SIGMA) was computed using the Graybill Wang method. Since the sample mean and mean squares for the between location and within location are independent, the overall α level (1- confidence level) is the product of the two individual α levels for μ and σ . So the two individual confidence levels are the square root of the overall α . Then the portion of the overall α used to estimate μ is divided equally to construct a 2-tailed test. Since the confidence interval for σ is one-sided, the portion of the overall α for σ is all put into one tail. [Note that SM is not the between location variance component. It's the standard deviation of the location means.] Then, for increasing values of the sample mean starting at 84.9, the lower bound is calculated by calling the macro *cullu*. Once the lower bound (OVERBDL) is greater than the specified lower bound (LBOUND), the lower limit for the sample mean has been identified (MEANL) and program goes to the label UPPER to find the upper limit for the sample mean. This time the sample mean starts at 115.1, calls the macro *cuulu*, and decreases until the overall bound (OVERBU) is greater than LBOUND. The upper bound for the mean (MEANU) has been identified. So for the given values for SE and SM, the lower and upper limits for the sample mean have been found.

The SAS code is written to handle two special situations. The first is when the value of SM equals D (D is the starting value for both SM and SE in the DO loops). If SM equals D, this means that for the first value of SM, the upper bound was greater than the specified lower bound. Therefore, there is no sample mean that results in an evaluated lower bound less than the specified bound. The symbol '!' is output indicating that there is no sample mean that meets the requirements for the lower bound and confidence level specified. The second situation is if SE equals D. This means that the largest value of SM that needs to be evaluated anywhere in the table has been found. So, the code resets the largest value of SM that needs to be evaluated.

The set of means and standard deviations is stored in the data set TABC.

PRTCUSP2 [259-442]

This macro prints the acceptance limit table by reading the data set TABC, transposing it, and printing out data.

EVCUSP2 [443-479]

The between location standard deviation is the between location variance component and not the standard deviation of the location means. For the population mean, the user specifies the lower bound for the mean (ULOW), the upper bound for the mean (UHIGH), the increment (UINCRE), and the divisor (UDIV). Each of these values must be a positive integer. So if the user wants to evaluate population means from 98.0 to 102.0 by 0.5, the following values would be specified: ULOW = 980, UHIGH = 1020, UINCRE = 5, and UDIV = 10. The upper and lower values for the within location standard deviation and between location standard deviation as well as the increment and divisor are input in the same manner as those for the mean.

The macro *SIGCUSP2* performs the calculations for each population mean (U), within location standard deviation (SIGSE), between location standard deviation (SIGSM) combination. The strategy is as follows: The acceptance limit table consists of a pair of sample means for each combination of within location standard deviation (SE) and standard deviation of location means (SM). Data set TABC contains the lower limit for the sample mean (MEANL), the upper limit for the sample mean (MEANU), the value of the within location standard deviation (SE), and the standard deviation of the between location means (SM). To calculate the probability of passing the acceptance limit tables for specified values for the population mean, within location standard deviation, and between location standard deviation, the probability is calculated of a sample mean falling between the upper and lower mean limits. So, suppose one line from TABC is $se = 0.4$, $sm = 0.2$, $meanl = 98.0$, and $meanu = 101.5$. Then the program would calculate the probability that the sample mean would lie within 98.0 and 101.5, se would lie between 0.3 and 0.4, and sm would lie between 0.1 and 0.2. This is done using the SAS functions - PROBNORM and PROBCHI. The same calculation would be performed for each observation in the data set TABC. These probabilities are summed for all observation in the data set. The sum of these probabilities (PSUM) is the probability of passing the table for specific population values for the mean, within and between location standard deviations. The last value of PSUM is output. PROC APPEND is used to save the PSUM value for each combination of U, SIGSE, and SIGSM in the DO loop. These values are stored in the data set SAVES2E. Finally, the data set SAVES2E is printed.

SMPCUSP2 [480-517]

This macro is used to calculate the lower bound of passing the USP content uniformity test given the sample mean, sample within location standard deviation, and the standard deviation of location means. The data set TAB determines the endpoints of the confidence interval based on the user input values for the sample mean, sample within location standard deviation, and standard deviation of location means and prior information such as dosage form type, confidence level,

number of locations and number of samples at each location. The overall α is divided into two portions as described in the macro *calcusp2*. The macro's *cullu* and *cuulu* are called to determine the lower bound. Finally, the lower bound is printed.

ANACUSP2 [518-534]

This macro is used to respond to the user input from the chosen initial test/sampling plan window. If the user requests printing of the acceptance limit table or evaluation of a table, then the macro *calcusp2* is called. If the user requests a printout of the acceptance limit table, the macro *PRTCUSP2* is called. If an evaluation is requested, the macro *EVCUSP2* is called. After the evaluation macro is finished the dataset SAVES2E is deleted. Finally, if the user requests a lower bound for a sample mean and standard deviation, the macro *SMPCUSP2* is called.

PROGRAM: DISP1.SAS - Used to generate Dissolution acceptance limits using Sampling Plan 1

The macros contained in DISP1.SAS are defined below:

COMPUTE [51-63]

For specific values of the population mean and standard deviation, this macro performs the lower probability bound calculation.

Each time this macro is called there is one value for μ (LLU) and one value for σ (SIGMA). The pair LLU, SIGMA is evaluated. PROBNORM is used to calculate the normal probability of an individual value falling within a given interval. Since the probability of passing the USP test is greater than or equal to the probability of passing any individual stage, the maximum probability of passing is selected from stage 1 (F1), stage 2 (F2), and stage 3 (F3).

caldisp1 [64-108]

This macro finds the acceptance limit on the CV for a given sample mean. The confidence interval is a triangle. For dissolution, only one point needs to be evaluated. This is the point with the smallest value of the population mean and the maximum value of sigma. So, for a given value of the sample mean, one can just keep increasing the sample value of the standard deviation until the evaluation of the point on the triangle has a lower bound probability less than pre-specified lower bound. Also note that the probability of passing the dissolution test only depends on the distance from Q and not the actual value of Q. So, the lower bound on passing the dissolution test with a Q of 80 and sample mean of 85 would be the same as passing the dissolution test with a Q of 85 and a sample mean of 90 since they both are 5 units away from Q. Therefore, this macro generates the acceptance limits on the interval from 0 to (100 - Q). Once the table has been generated, the value of Q is added to each value of the sample mean. The table is generated by using a DO loop that starts with a sample mean of 0.2 and goes to (100 - Q) in increments of 0.2 (set by macro variable D). The standard deviation starts at 0.002 (STARTSD) and increments by 0.001. For each value of the standard deviation (SAMPSTD), the upper bound for sigma (SIGMA) is calculated using the usual confidence bound formula. The point in the confidence interval that will be evaluated is determined (LLU). LLU is the lower end of the confidence region associated with SIGMA. Since the sample mean and sample variance are independent, the overall α level (1- confidence level) is the product of the two individual α levels for μ and σ . So each of the two individual confidence levels are the square root of the overall α . The macro *COMPUTE* is called to find the lower bound on the probability of passing the USP test for LLU. If the minimum is greater than the lower bound selected by the user (LBOUND), the standard deviation (SAMPSTD) is incremented by 0.001 and a new LLU is computed and the minimum probability is found again. Once the minimum is less

than the lower bound, 0.001 is subtracted from the standard deviation, and the CV is computed. A special case is when the starting value (STARTSD) of 0.002 gives a minimum less than the lower bound. In this case the CV is set to 0. The value of the standard deviation is used as a starting point for the next sample mean since we know that the standard deviation must increase as the sample mean increases.

Once the entire set of sample mean, CV combinations are determined, the data is sorted by MEAN and a data set is prepared for use in printing the table. This is done by creating five data sets. Each of these data sets contains the data for two columns of the printed acceptance table. Data set ONE contains the mean and CV for the first fifth of the values of the sample mean, data set TWO the second fifth, etc. All five of these data sets are then merged together to form data set D1ALL.

PRTDISP1 [109-123]

This macro prints the acceptance limit table by printing out data set D1ALL prepared by the macro *caldisp1*.

EVDISP1 [124-146]

For the population mean, the user specifies the lower bound for the mean (ULOW), the upper bound for the mean (UHIGH), the increment (UINCRE), and the divisor (UDIV). Each of these values must be a positive integer. So if the user wants to evaluate population means from 90.0 to 92.0 by 0.5, the following values would be specified: ULOW = 900, UHIGH = 920, UINCRE = 5, and UDIV = 10. The upper and lower values for the CV as well as the increment and divisor are input in the same manner as those are for the mean. Finally, data set D1ALL is read into data set DI1SET. The macro DSCUSP1 reads DI1SET and creates five data sets containing the sample means and standard deviations from DI1SET. The five data sets are appended to one another and stored in data set DIONE.

The macro *SIGDISP1* performs the calculations for each population mean and CV combination. The strategy is as follows: The acceptance limit table consists of pairs of sample means with an upper bound on the sample CV. Data set DIONE contains the sample mean and sample standard deviation pairs that make up the entire acceptance limit table beginning with a sample mean of $Q + 0.2$ and ending with a sample mean of 100.0. To calculate the probability of passing the acceptance limit table for specified values for the population mean and population CV, the probability is calculated of a sample mean falling between adjacent means in the table and the sample standard deviation falling below the average standard deviation at the two endpoints. The product of these two probabilities is computed since the sample mean and sample variance are independent of one another. So, suppose the standard deviation at a sample mean of 75.2 was 0.2 and the sample standard deviation bound at a sample mean of 75.4 was 0.5. If the evaluation was at a population mean of 100 with standard deviation of 3, then the

first calculation would be to find the probability of getting a sample mean between 75.2 and 75.4 and a sample standard deviation less than $(0.2 + 0.5)/2$ or 0.35. This is done using the SAS functions - PROBNORM and PROBCHI. The second calculation would calculate the probability of getting a sample means between 75.4 to 75.6 with a sample standard deviation less than the average of the corresponding standard deviations for 75.4 and 75.6. These probabilities are summed across all the intervals from $Q + 0.2$ to 100.0. The sum of these probabilities (PTRAP) is the probability of passing the table for specific population values for the mean and standard deviation. To perform the calculation, the lag function in SAS is used to obtain the previous value for the sample mean and sample standard deviation. The last value of PTRAP is output. PROC APPEND is used to save the PTRAP value for each combination of CV and U in the DO loop. These values are stored in the data set D1SAVALL. Finally, the data set D1SAVALL is printed.

SMPDISP1 [147-172]

This macro is used to calculate the lower bound of passing the USP dissolution test given the sample mean and sample standard deviation. The data set DI1SMP determines the endpoints of the confidence interval based on the user input values for the sample mean and standard deviation and prior information such as confidence level and sample size. The macro *COMPUTE* is called to determine the lower bound. Finally, the lower bound is printed.

ANADISP1 [173-188]

This macro is used to respond to the user input from the initial window chosen from the test/sampling plan window. If the user requests printing of the acceptance limit table or evaluation of a table, then the macro *caldisp1* is called. If the user requests a printout of the acceptance limit table, the macro *PRTDISP1* is called. If an evaluation is requested, the macro *EVDISP1* is called. After the evaluation macro is finished the dataset D1SAVALL is deleted. Finally, if the user requests a lower bound for a sample mean and standard deviation, the macro *SMPDISP1* is called.

PROGRAM: DISP2.SAS - Used to generate Dissolution acceptance limits using Sampling Plan 2

The macros contained in DISP2.SAS are defined below:

COMPUTE [121-133]

For specific values of the population mean and standard deviation, this macro performs the lower probability bound calculation.

Each time this macro is called there is one value for μ (LLU) and one value for σ (SIGMA). The pair LLU, SIGMA is evaluated. PROBNORM is used to calculate the normal probability of an individual value falling within a given interval. Since the probability of passing the USP test is greater than or equal to the probability of passing any individual stage, the maximum probability of passing is selected from stage 1 (F1), stage 2 (F2), and stage 3 (F3).

caldisp2 [137-198]

This macro finds the acceptance limit on the CV for a given mean. The confidence interval is a triangle. The only point to evaluate on the triangle is the point with the smallest value of the population mean and the maximum value of sigma. However, the value of sigma is a function of both the between and within variance components. The confidence interval for the sum of the within and between variance components uses the Graybill, F.A. & Wang, C. method described above in the macro *calcusp2* of the content uniformity section for sampling plan 2. Since the sample mean and mean squares for the between location and within location are independent, the overall α level (1- confidence level) is the product of the two individual α levels for μ and σ . So the two individual confidence levels are the square root of the overall α .

The strategy was as follows: Given the sample within location standard deviation (SE) and the sample between location standard deviation (SM), a confidence interval for σ (SIGMA) was computed using the Graybill Wang method. Then, for increasing values of the sample mean starting at 0.2, the lower bound was calculated by calling the macro *COMPUTE*. Once the lower bound (OVERBD) is greater than the specified lower bound (LBOUND), the lower limit for the sample mean has been found (MEANL) for the given values of SE and SM.

As described in *calcusp2*, the SAS code is written to handle two special situations when either the value of SM or SE equals D.

These values are stored in the data set TABD.

PRTDISP2 [200-218]

This macro prints the acceptance limit table using the SAS procedure PROC TABULATE by reading the data set TABD and printing the output.

EVDISP2 [221-362]

For the population mean, the user specifies the lower bound for the mean (ULOW), the upper bound for the mean (UHIGH), the increment (UINCRE), and the divisor (UDIV). Each of these values must be a positive integer. So if the user wants to evaluate population means from 90.0 to 92.0 by 0.5, the following values would be specified: ULOW = 900, UHIGH = 920, UINCRE = 5, and UDIV = 10. The upper and lower values for the within location standard deviation and between location standard deviation as well as the increment and divisor are input in the same manner as those for the mean.

The macro *SIGDISP2* [312-346] performs the calculations for each population mean (U), within location (SIGSE), between location (SIGSM) combination. The strategy is as follows: The acceptance limit table consists of a sample mean for each combination of within location standard deviation (SE) and standard deviation of location means (SM). Data set TABD contains the lower limit for the sample mean (MEANL), the value of the within location standard deviation (SE), and the standard deviation of the between location means (SM). To calculate the probability of passing the acceptance limit tables for specified values for the population mean, within location standard deviation, and between location standard deviation, the probability is calculated of a sample mean falling above lower mean limit. So, suppose one line from TABD is se = 0.4, sm = 0.2 and meanl = 98.0. Then the program would calculate the probability that the sample mean would be greater than 98.0, se would lie between 0.3 and 0.4, and sm would lie between 0.1 and 0.2. This is done using the SAS functions - PROBNORM and PROBCHI. The same calculation would be performed for each observation in the data set TABD. These probabilities are summed for all observation in the data set. The sum of these probabilities (PSUM) is the probability of passing the table for specific population values for the mean, within and between location standard deviations. The last value of PSUM is output. PROC APPEND is used to save the PSUM value for each combination of U, SIGSE, and SIGSM in the DO loop. These values are stored in the data set SAVES2E. Finally, the data set SAVES2E is printed.

SMPDISP2 [364-440]

This macro is used to calculate the lower bound of passing the USP dissolution test given the sample mean, sample within location standard deviation, and the standard deviation of location means. The data set TAB determines the endpoints

of the confidence interval based on the user input values for the sample mean, sample within location standard deviation, and standard deviation of location means and prior information such as confidence level, number of locations and number of samples at each location. The macro COMPUTE is called to determine the lower bound. Finally, the lower bound is printed.

ANADISP2 [442-456]

This macro is used to respond to the user input from the initial window selected from the test/sampling plan. If the user requests printing of the acceptance limit table or evaluation of a table, then the macro *caldisp2* is called. If the user requests a printout of the acceptance limit table, the macro *PRTDISP2* is called. If an evaluation is requested, the macro *EVDISP2* is called. After the evaluation macro is finished, the dataset SAVES2E is deleted. Finally, if the user requests a lower bound for a sample mean and standard deviation, the macro *SMPDISP2* is called.

APPENDIX G

TEST DATA

Content Uniformity
Sampling Plan 1
Test Data Set & Results

Target	CI Level	Lower Bound	Sample Size	Sample Mean	Program Result CV	Independent Result CV	Agree? (Y or N)
100	50.0	50.0	5	85.1			
				100.0			
				114.9			
			2000	85.1			
				100.0			
				114.9			
	99.0	50.0	5	85.1			
				100.0			
				114.9			
			2000	85.1			
				100.0			
				114.9			
	99.0	99.0	5	85.1			
				100.0			
				114.9			
			2000	85.1			
				100.0			
				114.9			
104.5	50.0	50.0	5	85.1			
				100.0			
				114.9			
			2000	85.1			
				100.0			
				114.9			
	50.0	99.0	5	85.1			
				100.0			
				114.9			
			2000	85.1			
				100.0			
				114.9			
	99.0	99.0	5	85.1			
				100.0			
				114.9			
			2000	85.1			
				100.0			
				114.9			

Content Uniformity
Sampling Plan 2
Test Data Set & Results

							Program	Independent	Program	Independent	All
Target	CI	Lower	# Loc	#/Location	SE	SM	Result	Result	Result	Result	Agree?
	Level	Bound					Mean	Mean	Mean	Mean	(Y or N)
							(Lower)	(Lower)	(Upper)	(Upper)	
100	50.0	50.0	3	2	0.1	0.1					
					0.1	3.0					
					3.0	0.1					
					3.0	3.0					
				300	0.1	0.1					
					0.1	3.0					
					3.0	0.1					
					3.0	3.0					
	50.0	99.0	300	2	0.1	0.1					
					0.1	3.0					
					3.0	0.1					
					3.0	3.0					
				300	0.1	0.1					
					0.1	3.0					
					3.0	0.1					
					3.0	3.0					
	99.0	99.0	3	2	0.1	0.1					
					3.0	3.0					
				300	0.1	0.1					
					0.1	3.0					
					3.0	0.1					
					3.0	3.0					
			300	300	0.1	0.1					
					0.1	3.0					
					3.0	0.1					
					3.0	3.0					
102.5	50.0	50.0	3	2	0.1	3.0					
	99.0	50.0	300	300	3.0	3.0					
	99.0	50.0	3	2	0.1	0.1					
				300	0.1	3.0					

ACCEPTANCE LIMITS FOR DISSOLUTION (N = 3, Q = 85.0)
 SAMPLING PLAN 1
 (MEETING LIMITS GUARANTEES WITH 50.0 % ASSURANCE,
 THAT AT LEAST 50.0% OF ALL FUTURE SAMPLES TESTED
 FOR DISSOLUTION WILL PASS THE USP TEST)
 TABLE ENTRY IS UPPER LIMIT ON CV OF 3 DISSOLUTION ASSAYS

MEAN (% CLAIM)	CV (%)	MEAN (% CLAIM)	CV (%)	MEAN (% CLAIM)	CV (%)	MEAN (% CLAIM)	CV (%)	MEAN (% CLAIM)	CV (%)
85.2	0.44	88.2	5.84	91.2	7.62	94.2	8.73	97.2	9.51
85.4	0.88	88.4	6.01	91.4	7.71	94.4	8.79	97.4	9.56
85.6	1.31	88.6	6.16	91.6	7.80	94.6	8.85	97.6	9.60
85.8	1.74	88.8	6.30	91.8	7.88	94.8	8.90	97.8	9.65
86.0	2.18	89.0	6.44	92.0	7.96	95.0	8.96	98.0	9.69
86.2	2.60	89.2	6.57	92.2	8.04	95.2	9.01	98.2	9.74
86.4	3.03	89.4	6.69	92.4	8.12	95.4	9.07	98.4	9.78
86.6	3.46	89.6	6.81	92.6	8.19	95.6	9.12	98.6	9.82
86.8	3.88	89.8	6.92	92.8	8.26	95.8	9.17	98.8	9.86
87.0	4.29	90.0	7.03	93.0	8.33	96.0	9.23	99.0	9.90
87.2	4.66	90.2	7.14	93.2	8.40	96.2	9.28	99.2	9.94
87.4	4.97	90.4	7.24	93.4	8.47	96.4	9.32	99.4	9.98
87.6	5.24	90.6	7.34	93.6	8.54	96.6	9.37	99.6	10.03
87.8	5.46	90.8	7.44	93.8	8.60	96.8	9.42	99.8	10.06
88.0	5.66	91.0	7.53	94.0	8.67	97.0	9.47	100.0	10.10

ACCEPTANCE LIMITS FOR DISSOLUTION (Q = 40.0)
SAMPLING PLAN 2
LOWER BOUND = 50.0, CONFIDENCE LEVEL = 99.0
TABLE ENTRIES ARE LOWER LIMITS ON THE MEAN
OF 6 ASSAYS- 2 ASSAYS AT EACH OF 3 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
SE								
0.25	45.30	50.60	57.30	66.00	76.70	88.10	99.70	
0.50	45.30	50.60	57.30	66.00	76.70	88.10	99.70	
0.75	45.30	50.60	57.30	66.00	76.70	88.10	99.70	
1.00	45.30	50.60	57.30	66.10	76.70	88.10	99.70	
1.25	45.30	50.70	57.40	66.20	76.80	88.20	99.80	
1.50	45.30	50.80	57.60	66.30	76.90	88.20	99.80	
1.75	45.50	51.10	57.90	66.50	77.00	88.30	99.90	
2.00	45.90	51.60	58.30	66.80	77.30	88.50	100.00	
2.25	46.60	52.20	58.90	67.30	77.60	88.70		
2.50	47.50	53.00	59.60	67.90	78.00	89.00		
2.75	48.50	54.10	60.60	68.70	78.50	89.30		
3.00	49.80	55.30	61.70	69.70	79.20	89.80		
3.25	51.30	56.80	63.10	70.80	80.00	90.30		
3.50	53.00	58.50	64.70	72.10	81.00	91.00		

3.75	54.90	60.30	66.40	73.60	82.10	91.80
4.00	56.80	62.20	68.20	75.10	83.30	92.70
4.25	58.80	64.20	70.00	76.70	84.60	93.70
4.50	60.80	66.20	71.90	78.50	86.10	94.80
4.75	62.80	68.20	73.90	80.30	87.60	96.10
5.00	64.90	70.20	75.90	82.10	89.20	97.40
5.25	67.00	72.30	77.90	84.00	90.90	98.80
5.50	69.10	74.40	79.90	85.90	92.70	
5.75	71.20	76.50	82.00	87.90	94.50	
6.00	73.30	78.60	84.00	89.90	96.30	
6.25	75.40	80.70	86.10	91.90	98.20	

J

(Continued)

ACCEPTANCE LIMITS FOR DISSOLUTION (Q = 40.0)
 SAMPLING PLAN 2
 LOWER BOUND = 50.0, CONFIDENCE LEVEL = 99.0
 TABLE ENTRIES ARE LOWER LIMITS ON THE MEAN
 OF 6 ASSAYS- 2 ASSAYS AT EACH OF 3 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
SE								
6.50	77.50	82.80	88.20	93.80	99.90			
6.75	79.30	84.60	90.00	95.60				
7.00	81.10	86.40	91.70	97.30				
7.25	82.90	88.20	93.50	99.10				
7.50	84.70	90.00	95.30					
7.75	86.50	91.80	97.10					
8.00	88.40	93.60	98.90					
8.25	90.20	95.40						
8.50	92.00	97.20						
8.75	93.80	99.10						
9.00	95.60							
9.25	97.40							
9.50	99.20							

FORMS

FORM 1

LOAD AND RUN PROGRAM

Name: _____

Computer Description:

PC

Manufacturer: _____

Model: _____

CPU Speed: _____

Hard Drive Size: _____

RAM Memory: _____

SAS Version Number: _____

Sign below to indicate that the program, CuDAL, loaded and ran successfully on your PC.

Name _____ Date: _____

FORM 2

PRIMARY WINDOW NAVIGATION & INPUT ERROR CHECKS

Sign below to indicate that all of the found responses agree with the expected results in Appendix D.

Name: _____ Date: _____

Navigation & Window Input Error Checking Lead

FORM 3

MATHEMATICAL CALCULATION VERIFICATION

Signing below indicates that the calculations described in Appendix E to determine lower bounds for content uniformity are correct.

Name: _____ Date: _____

Macro Strategy, SAS Code & Mathematical Calculation Lead

FORM 4

PROGAM STRATEGY & SAS CODE VERIFICATION

Signing below indicates the following:

- 1) The calculations described in Appendix E to determine lower bounds for content uniformity and dissolution are implemented correctly in the macros.
- 2) The strategies described in Appendix F are appropriate.
- 3) The SAS code implements the strategies described in Appendix F correctly.

Name: _____ Date: _____

Macro Strategy, SAS Code & Mathematical Calculation Lead

FORM 5

TEST DATA SET AGREEMENT

Test Table generation

Signing below indicates that for the test data in Appendix G, CuDAL results agree with the results of independent calculations for content uniformity and are identical to the tables generated by version 1 for dissolution.

Name: _____ Date: _____

Test Data Evaluation & Independent Calculations Lead

FORM 6
PROBLEM/REQUEST REPORT

Name: _____

Date: _____

Describe the error or discrepancy in expected result verses found result or in expected performance of the program.

Amendment 1

Name: James Bergum

Date: May 31, 2007

Description:

Several misprints were found on pages 98-101, Appendix E, of the validation protocol. The revised pages are attached. These revisions only pertain to the protocol and do not affect the SAS programs. Revisions are shown in **BOLD**. Deletions are described in a text box.

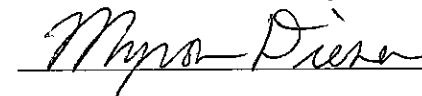
Summary of changes:

- 1) Two density functions were given the same name, f . To eliminate confusion, they were revised to f_1 and f_2 .
- 2) The parameter in f_2 is r but was defined using γ . γ was replaced by r .
- 3) h was used in two ways: a function name and the interval width for integration. Therefore h was changed to H for the function name. Since a capitol letter was used for H , the function g was renamed G .
- 4) The numerical integration used arguments z_1 and z_2 for I_2 and I_3 . The arguments should have used 101.5 and 98.5-15 for I_2 and I_3 , respectively. Also, in the second set of numerical integration expressions, the function f was replaced by Φ .
- 5) In the calculation of $P(C_{22})$, the \sqrt{n} was removed since the calculation is for an individual result.

Validation Team Lead Approval:

Yijie Dong:  07/10/2007

Merlin Utter:  07/25/2007

Myron Diener:  8/2/07

For $T \leq 101.5$,

$$\begin{aligned} P(S_1) = & P(98.5 \leq \bar{X} \leq 101.5 \text{ and } k_1 s < L_1) \\ & + P(\bar{X} > 101.5 \text{ and } \bar{X} - 101.5 + k_1 s < L_1) \\ & + P(\bar{X} < 98.5 \text{ and } 98.5 - \bar{X} + k_1 s < L_1), \end{aligned}$$

where $k_1 = 2.4$.

By the central Limit Theorem, $\bar{X} = \frac{1}{n} \sum_{i=1}^n X_i$ follows a normal distribution with mean μ and standard deviation σ / \sqrt{n} denoted as $N(\mu, \sigma / \sqrt{n})$. Also $(n-1)s^2/\sigma^2$ follows a χ^2 distribution with $n-1$ degrees of freedom where

$$\text{standard deviation } s = \sqrt{\frac{1}{n-1} \sum_{i=1}^n (X_i - \bar{X})^2}$$

\bar{X} and S^2 are independent variables. The joint density of (\bar{X}, s^2) can be calculated by the product of their densities.

Denote $Z_1 = \bar{X}$ and $Z_2 = (n-1)s^2/\sigma^2$.

The density functions $f_1(Z_1)$ and $f_2(Z_2)$ are

$$f_1(Z_1 = z_1) = \frac{1}{\sigma \sqrt{2\pi}} e^{-\frac{(z_1 - \mu)^2}{2\sigma^2}}$$

$$f_2(Z_2 = z_2) = \frac{1}{\Gamma(r/2) 2^{r/2}} z_2^{r/2-1} e^{-z_2/2} \text{ for } z_2 \geq 0.$$

where $r = n-1$ and $\Gamma(p) = \int_0^\infty t^{p-1} e^{-t} dt$.

The density function of Z_2 is a Chi-Square distribution with $n-1$ degrees of freedom and is denoted as $\chi^2_{(n-1)}$.

The joint density function is $f(z_1, z_2) = f_1(z_1) f_2(z_2)$,

Due to the independency of Z_1 and Z_2 , $P(S_1)$ in terms of Z_1 and Z_2 , can be rewritten as

$$\begin{aligned} P(S_1) = & P(98.5 \leq Z_1 \leq 101.5 \text{ and } k_1 \sigma \sqrt{\frac{Z_2}{(n-1)}} < L_1) \\ & + P(Z_1 > 101.5 \text{ and } Z_1 - 101.5 + k_1 \sigma \sqrt{\frac{Z_2}{(n-1)}} < L_1) \end{aligned}$$

$$\begin{aligned}
& + P(Z_1 > 101.5 \text{ and } Z_1 - 101.5 + k_1 \sigma \sqrt{\frac{Z_2}{(n-1)}} < L_1) \\
& + P(Z_1 < 98.5 \text{ and } 98.5 - Z_1 + k_1 \sigma \sqrt{\frac{Z_2}{(n-1)}} < L_1) \\
& = I_1 + I_2 + I_3,
\end{aligned}$$

where

$$\begin{aligned}
I_1 &= P(98.5 \leq Z_1 \leq 101.5 \text{ and } k_1 \sigma \sqrt{\frac{Z_2}{(n-1)}} < L_1) \\
I_2 &= P(Z_1 > 101.5 \text{ and } Z_1 - 101.5 + k_1 \sigma \sqrt{\frac{Z_2}{(n-1)}} < L_1) \\
I_3 &= P(Z_1 < 98.5 \text{ and } 98.5 - Z_1 + k_1 \sigma \sqrt{\frac{Z_2}{(n-1)}} < L_1)
\end{aligned}$$

Notice that

$$\begin{aligned}
I_1 &= P(98.5 \leq Z_1 \leq 101.5) * P(k_1 \sigma \sqrt{\frac{Z_2}{(n-1)}} < L_1) \\
&= (\Phi(t_1) - \Phi(t_2)) * P(Z_2 < (n-1) * L_1^2 / (k_1^2 \sigma^2))
\end{aligned}$$

with $t_1 = \sqrt{n}(101.5 - \mu) / \sigma$ and $t_2 = \sqrt{n}(98.5 - \mu) / \sigma$

and Φ the cumulative density function of standard normal $N(0,1)$.

Let $G(z_1) = (n-1) * (L_1 + 101.5 - z_1)^2 / (k_1 \sigma)^2$. Noting that that $L_1 = 15$, we have

$$\begin{aligned}
I_2 &= P(Z_1 > 101.5 \text{ and } Z_2 < G(Z_1)) \\
&= \int_{101.5}^{101.5+15} f_1(z_1) \int_0^{G(z_1)} f_2(z_2) dz_2 dz_1
\end{aligned} \tag{1}$$

Let $H(z_1) = (n-1)(L_1 - 98.5 + z_1)^2 / (k_1 \sigma)^2$. Then

$$I_3 = P(Z_1 < 98.5 \text{ and } Z_2 < H(Z_1))$$

The integrations of (1) and (2) have no analytical results due to the complexities of their integrands. However, numerical results of the integrations can be calculated. For a Chi-Square distribution with k degrees of freedom, the function PROBCHI(y,k) in SAS provides the numerical result of integration $\int_0^y f(z_2) dz_2$ for given y. Taking advantage of known function PROBCHI(y,k), the numerical integrations of (1) and (2) are calculated as follows:

$$I_2 = \lim_{h \rightarrow 0} \sum_{i=1}^K (\Phi(101.5 + ih) - \Phi(101.5 + (i-1)h)) \text{PROBCHI}(G(101.5 + (i-1/2)h), n-1)$$

where $K = \lceil L_1/h \rceil$, the number of intervals of width h. Similarly, for I_3 ,

$$I_3 = \lim_{h \rightarrow 0} \sum_{i=1}^K (\Phi(98.5-15 + ih) - \Phi(98.5-15 + (i-1)h)) \text{PROBCHI}(H(98.5-15 + (i-1/2)h), n-1)$$

A small program in SAS can be programmed to carry out the calculation. Therefore, $P(S_1)$ can be calculated as

$$P(S_1) = (\Phi(t_1) - \Phi(t_2)) * P(Z_2 < (n-1) * L_1^2 / (k_1^2 \sigma^2)) + I_2 + I_3$$

A similar calculation can be performed for $T > 101.5$ by replacing 101.5 in the above equations with T.

Computation of $P(S_2)$ There are two sub-criteria in S_2 which are denoted as C_{21} and C_{22} respectively as follows:

C_{21} = AV of the 30 dosage units is less than or equal to L_1 .

C_{22} = No unit is over the deviation of L_2 from the calculated value of M.

Using the inequality that, for two events A and B,

$$P(A \text{ and } B) = P(A) + P(B) - P(A \text{ or } B) \geq P(A) + P(B) - 1.$$

One gets $P(S_2) = P(C_{21} \text{ and } C_{22}) \geq \max\{P(C_{21}) + P(C_{22}) - 1, 0\}$

Since criteria C_{21} is very similar to S_1 except for $n=30$ and $k=2.0$ in the former while $n=10$ and $k=2.4$ in the later, the calculation of $P(C_{21})$ is carried out similarly as in $P(S_1)$ with $n=30$ and $k=2.0$. Therefore,

$$P(C_{21}) = (\Phi(t_1) - \Phi(t_2)) * P(Z_2 < (n-1) * L_1^2 / (k_2^2 \sigma^2))$$

$$\begin{aligned}
& + \lim_{h \rightarrow 0} \sum_{i=1}^K (\Phi(101.5 + ih) - \Phi(101.5 + (i-1)h)) \text{PROBCHI}(G(101.5 + (i-1/2)h), n-1) \\
& + \lim_{h \rightarrow 0} \sum_{i=1}^K (\Phi(98.5-15 + ih) - \Phi(98.5-15 + (i-1)h)) \text{PROBCHI}(H(98.5-15 + (i-1/2)h), n-1)
\end{aligned}$$

where $n = 30$ and $k_2 = 2.0$. For the calculation of $P(C_{22})$, notice that

For $T \leq 101.5$

$$M = \begin{cases} 98.5 & \text{if } \bar{X} < 98.5 \\ \bar{X} & \text{if } 98.5 \leq \bar{X} \leq 101.5 \\ 101.5 & \text{if } \bar{X} > 101.5 \end{cases}$$

Then, with $L_2 = 25$,

$$\begin{aligned}
P(C_{22}) &= P(98.5 \leq \bar{X} \leq 101.5 \text{ and } |X_i - \bar{X}| < L_2, i = 1, \dots, n) \\
&+ P(\bar{X} > 101.5 \text{ and } |X_i - 101.5| < L_2, i = 1, \dots, n) \\
&+ P(\bar{X} < 98.5 \text{ and } |X_i - 98.5| < L_2, i = 1, \dots, n) \\
&= P(98.5 \leq \bar{X} \leq 101.5 \text{ and } \bar{X} - L_2 < X_i < \bar{X} + L_2, i = 1, \dots, n) \\
&+ P(\bar{X} > 101.5 \text{ and } 101.5 - L_2 < X_i < 101.5 + L_2, i = 1, \dots, n) \\
&+ P(\bar{X} < 98.5 \text{ and } 98.5 - L_2 < X_i < 98.5 + L_2, i = 1, \dots, n) \\
&\geq P(101.5 - L_2 < X_i < 98.5 + L_2, i = 1, \dots, n) \\
&= [\Phi((98.5 + L_2 - \mu)/\sigma) - \Phi((101.5 - L_2 - \mu)/\sigma)]^n
\end{aligned}$$

For $T > 101.5$

Removed \sqrt{n}

Amendment 2

Name: James Bergum

Date: June 2, 2007

Description:

This amendment addresses two errors found in the program. Neither error involves the calculations.

Error 1: The CuDAL logo did not appear on the opening screen. There were two reasons for this error: 1) The logo was not included with the program sent to the validation team. and 2) The navigation/error checking code contained a specific 'hard coded' directory location for the logo. This would force the user to create a directory for the logo that was the same as the 'hard coded' directory. Code was added to the opening program (CuDAL.SAS) that allows the user to specify the location of the logo. The revised CuDAL.SAS code is attached and replaces the CuDAL.SAS code given in Appendix A of the protocol (p. 15). The appropriate changes were also made to the internal code to allow for flexibility of logo file location.

Error 2: In all four Test/Sampling plan combinations, an error screen appeared after entering an acceptable mean for the case where the user wanted to calculate the lower bound for a specific sample result. The two content uniformity test/sampling plan combinations should indicate an error if the sample mean is not in the interval 85.1 to 114.9. The two dissolution test/sampling plan combinations should indicate an error if the sample mean is not in the interval Q to 100. However, the error checking part of the program was checking the sample mean against both criteria (85.1 to 114.9 and Q to 100) no matter which test/sampling plan combination was selected. The program was modified so that only the 85.1 to 114.9 was used for content uniformity and Q to 100 was used for dissolution.

Validation Team Lead Approval:

Yijie Dong: *Yijie Dong* 07/10/2007

Merlin Utter: *Merlin Utter* 6/26/2007

Myron Diener: *Myron Diener* 6/12/07

CuDAL.SAS

```
1. ***** LIBRARY FOR THE APPLICATION*****;
2. /* deleting the macro variables */
3. data vars;
      i. set sashelp.vmacro;
4. run;
5. data _null_;
      i. set vars;
      ii. if scope='GLOBAL' and name ^= 'SYSODSPATH' then
      iii. call execute('%syndel '||trim(left(name))||';');
6. run;

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

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

Amendment 3

Name: James Bergum

Date: August 23, 2007

Description:

This amendment corrects a misinterpretation of the USP Content Uniformity test that requires revisions to the SAS programs Cusp1.sas and Cusp2.sas and the protocol. In Stage 2 of the USP test, the 2nd criteria is that no dosage unit can be more than **25% of M**. However, in the protocol and SAS programs, the criterion used was $M \pm 25$. If M is not 100, these two values are different. The correction to the program has minor impact on the results. Several revisions to the protocol were necessary. Revisions to both the program and protocol are attached.

Validation Team Lead Approval:

Yijie Dong: *Yijie Dong* *Aug 27, 2007*

Merlin Utter: *Merlin Utter* *Sept 6, 2007*

Myron Diener: *Myron Diener* *9/19/07*

SAS Program Revisions:

The following revision to the SAS code was done in two separate locations in each of the following SAS programs: Cusp1.sas and Cusp2.sas. In Cusp1.sas, both revisions were in the macro c1calc. In Cusp2, one revision was in the macro cullu and the other in the macro cuulu.

Replaced

```
zzz1=(123.5-mu)/sigma;  
if TARGET LE 101.5 then zzz2=(101.5-25-mu)/sigma;  
else zzz2 = (TARGET-25-mu)/sigma;
```

With

```
zzz1=(123.125-mu)/sigma;  
if TARGET LE 101.5 then zzz2=(101.5-24.625-mu)/sigma;  
else zzz2 = (TARGET-24.625-mu)/sigma;
```

Protocol Revisions

1) In Appendix A, revise the SAS code (described above) in the program listing at the following locations: (Lines 102-104 and 155-157 in Cusp1.sas; Lines 113-115 and 171-173 in Cusp2.sas)

2) Appendix C Default Window Output for Content Uniformity - Both Sampling Plans.

Replace with the attached output.

3) Appendix E

i) On page 96 of protocol, replace

Let $L_1 = 15$ and $L_2 = 25$. The criteria of S_1 and S_2 are as follows:

S_1 = The acceptance value (defined below) of the first 10 dosage units is $\leq L_1$

S_2 = i) The acceptance value of the 30 dosage units is $\leq L_1$

ii) No dosage unit is outside the maximum allowed range, L_2 , which is the deviation of each dosage unit tested from the calculated value of M (defined below).

With

Let $L_1 = 15$. The criteria of S_1 and S_2 are as follows:

S_1 = The acceptance value (defined below) of the first 10 dosage units is $\leq L_1$

- $S_2 =$
- i) The acceptance value of the 30 dosage units is $\leq L_1$
 - ii) No dosage unit deviates from the calculated value of M (defined below) by more than 25% of M

ii) On page 100 of protocol, Replace

C_{22} = No unit is over the deviation of L_2 from the calculated value of M.

With

C_{22} = No unit deviates from the calculated value of M by more than 25% of M.

iii) On page 101 of protocol, replace

Then, with $L_2 = 25$,

$$\begin{aligned}
 P(C_{22}) &= P(98.5 \leq \bar{X} \leq 101.5 \text{ and } |X_i - \bar{X}| < L_2, i = 1, \dots, n) \\
 &\quad + P(\bar{X} > 101.5 \text{ and } |X_i - 101.5| < L_2, i = 1, \dots, n) \\
 &\quad + P(\bar{X} < 98.5 \text{ and } |X_i - 98.5| < L_2, i = 1, \dots, n) \\
 &= P(98.5 \leq \bar{X} \leq 101.5 \text{ and } \bar{X} - L_2 < X_i < \bar{X} + L_2, i = 1, \dots, n) \\
 &\quad + P(\bar{X} > 101.5 \text{ and } 101.5 - L_2 < X_i < 101.5 + L_2, i = 1, \dots, n) \\
 &\quad + P(\bar{X} < 98.5 \text{ and } 98.5 - L_2 < X_i < 98.5 + L_2, i = 1, \dots, n) \\
 &\geq P(101.5 - L_2 < X_i < 98.5 + L_2, i = 1, \dots, n) \\
 &= [\Phi((98.5 + L_2 - \mu)/\sigma) - \Phi((101.5 - L_2 - \mu)/\sigma)]^n
 \end{aligned}$$

With

Then

$$\begin{aligned}
 P(C_{22}) &\geq P(98.5 \leq \bar{X} \leq 101.5 \text{ and } |X_i - \bar{X}| < 0.25 \cdot 98.5, i = 1, \dots, n) \\
 &\quad + P(\bar{X} > 101.5 \text{ and } |X_i - 101.5| < 0.25 \cdot 101.5, i = 1, \dots, n) \\
 &\quad + P(\bar{X} < 98.5 \text{ and } |X_i - 98.5| < 0.25 \cdot 98.5, i = 1, \dots, n) \\
 &= P(98.5 \leq \bar{X} \leq 101.5 \text{ and } \bar{X} - 24.625 < X_i < \bar{X} + 24.625, i = 1, \dots, n) \\
 &\quad + P(\bar{X} > 101.5 \text{ and } 101.5 - 25.375 < X_i < 101.5 + 25.375, i = 1, \dots, n) \\
 &\quad + P(\bar{X} < 98.5 \text{ and } 98.5 - 24.625 < X_i < 98.5 + 24.625, i = 1, \dots, n) \\
 &\geq P(101.5 - 24.625 < X_i < 98.5 + 24.625, i = 1, \dots, n)
 \end{aligned}$$

$$= [\Phi((98.5 + 24.625 - \mu)/ \sigma) - \Phi((101.5 - 24.625 - \mu)/ \sigma)]^n$$

iv) On page 102 of protocol, replace

Then, with $L_2 = 25$,

$$\begin{aligned} P(C_{22}) &= P(98.5 \leq \bar{X} \leq T \quad \text{and } |X_i - \bar{X}| < L_2, i = 1, \dots, n) \\ &\quad + P(\bar{X} > T \quad \text{and } |X_i - T| < L_2, i = 1, \dots, n) \\ &\quad + P(\bar{X} < 98.5 \quad \text{and } |X_i - 98.5| < L_2, i = 1, \dots, n) \\ &= P(98.5 \leq \bar{X} \leq T \quad \text{and } \bar{X} - L_2 < X_i < \bar{X} + L_2, i = 1, \dots, n) \\ &\quad + P(\bar{X} > T \quad \text{and } T - L_2 < X_i < T + L_2, i = 1, \dots, n) \\ &\quad + P(\bar{X} < 98.5 \quad \text{and } 98.5 - L_2 < X_i < 98.5 + L_2, i = 1, \dots, n) \\ &\geq P(T - L_2 < X_i < 98.5 + L_2, i = 1, \dots, n) \\ &= [\Phi((98.5 + L_2 - \mu)/ \sigma) - \Phi((T - L_2 - \mu)/ \sigma)]^n \end{aligned}$$

With

Then

$$\begin{aligned} P(C_{22}) &\geq P(98.5 \leq \bar{X} \leq T \quad \text{and } |X_i - \bar{X}| < 0.25*98.5, i = 1, \dots, n) \\ &\quad + P(\bar{X} > T \quad \text{and } |X_i - T| < 0.25*T, i = 1, \dots, n) \\ &\quad + P(\bar{X} < 98.5 \quad \text{and } |X_i - 98.5| < 0.25*98.5, i = 1, \dots, n) \\ &= P(98.5 \leq \bar{X} \leq T \quad \text{and } \bar{X} - 24.625 < X_i < \bar{X} + 24.625, i = 1, \dots, n) \\ &\quad + P(\bar{X} > T \quad \text{and } T - 0.25*T < X_i < T + 0.25*T, i = 1, \dots, n) \\ &\quad + P(\bar{X} < 98.5 \quad \text{and } 98.5 - 24.625 < X_i < 98.5 + 24.625, i = 1, \dots, n) \\ &\geq P(T - 24.625 < X_i < 98.5 + 24.625, i = 1, \dots, n) \\ &= [\Phi((98.5 + 24.625 - \mu)/ \sigma) - \Phi((T - 24.625 - \mu)/ \sigma)]^n \end{aligned}$$

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

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

92.9	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
93.0	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
93.1	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
93.2	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
93.3	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
93.4	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
93.5	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
93.6	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
93.7	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																		
SE	0.1		0.2		0.3		0.4		0.5		0.6		0.7		0.8		0.9	
	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

STANDARD DEVIATIONS AND MEANS ARE EXPRESSED IN % CLAIM

[illegible]

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																		
1.9			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	BETWEEN LOCATION	PROBABILITY
		STD DEV	STD DEV	OF
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

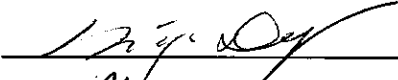


Amendment 4

Name: James Bergum
Date: September 24, 2007

Description:

One of the input error checks for dissolution tests that an error window is generated if the sample mean is less than Q or greater than 100. Problem/Request form 6 (Myron Diener dated 6/13/07) indicated that for a Q of 75 using sampling plan 1, a sample mean of 75 did not result in an error screen. For Q of 60 using sampling plan 2, a sampling mean of 60 did not result in an error screen. The protocol indicated that an error screen should have been generated. However, the program performed correctly since the mean was not less than Q. To test that the program will generate an error screen for means less than Q, the input error test data for these two cases have been changed from 75.0 to 74.9 and from 60.0 to 59.9 for dissolution sampling plans 1 and 2, respectively. In addition, the test cases using a mean of 100 have been changed to 100.1 to test that an error screen is generated when the sample mean is greater than 100. The revised test cases are attached.

Validation Team Lead Approval:

Yijie Dong:  10/19/2007
Merlin Utter:  10/17/2007
Myron Diener:  9/25/07

**APPENDIX D
WINDOW INPUT ERROR
CHECKING
TEST DATA**

**DISSOLUTION
SAMPLING PLAN 1**

Window	Requested Input	User Input	EXPECTED RESPONSE	FOUND RESPONSE	AGREE? (Y or N)
			N = NONE	N or ES	
			ES = ERROR SCREEN		
Lower Bound Based on Sample Result	Sample Mean	75.1	N		
	(Q = 75)	100.1	ES		
		85.5	N		
		74.9	ES		

**DISSOLUTION
SAMPLING PLAN 2**

Window	Requested Input	User Input	EXPECTED RESPONSE	FOUND RESPONSE	AGREE? (Y or N)
			N = NONE	N or ES	
			ES = ERROR SCREEN		
Lower Bound Based on Sample Result	Sample Mean	60.1	N		
	(Q = 60)	100.1	ES		
		80.6	N		
		59.9	ES		

Amendment 5

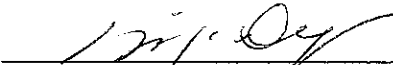

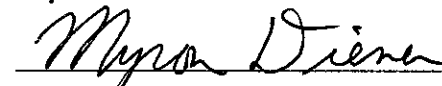
Name: James Bergum

Date: October 2, 2007

Description:

Two errors were found in the SAS code upon review of a Problem/Request report generated during the independent validation. A calculation used to calculate the difference in two probabilities for the 2nd criteria in Stage 2 of the USP test was incorrect. The subtraction was performed in the wrong order. Also found during the review was either a missing or misplaced statement in the programs Cusp1.sas and Cusp2.sas to define the variable "Target" from the macro variable T. Corrections to the program and changes to the protocol are attached. The corrected program will be rerun and compared to the independent program results to insure agreement between the two programs.

Validation Team Lead Approval:

Yijie Dong:  10/19/2007
Merlin Utter:  10/17/2007
Myron Diener:  10/18/2007

SAS Program Revisions:

The following revision to the SAS code was done in two separate locations in each of the following SAS programs: Cusp1.sas and Cusp2.sas. In Cusp1.sas, both revisions were in the macro c1calc. In Cusp2, one revision was in the macro cullu and the other in the macro cuulu.

Replaced

```
P2b=(probnorm(zzz2)-probnorm(zzz1))**30;
```

With

```
P2b=(probnorm(zzz1)-probnorm(zzz2))**30;
```

The following revisions were made to the SAS code:

In Cusp1.sas, the code: "TARGET = &T;" was moved to the following locations:

```
%macro c1calc;  
TARGET = &T;  
mu=LLU;
```

In Cusp2.sas, the code: "TARGET = &T;" was inserted at the following locations:

```
%macro cullu;  
  LLU = MEAN - Z * SQRT(MVAR / N);  
TARGET = &T;
```

```
%MACRO cuulu;  
  ULU = MEAN + Z * SQRT(MVAR / N);  
TARGET = &T;
```

Protocol Revisions

In Appendix A, the SAS code (described above) in the program listing was revised at the following locations:

- 1.) Edited lines 105 and 158 in Cusp1.sas and lines 116 and 174 in Cusp2.sas
- 2.) Deleted lines 169 and 174 and then inserted the new line of code (see above) after line 52 in Cusp1.sas. Inserted a new line of code (see above) after lines 63 and 121 in Cusp2.sas.

Appendix C for content uniformity was regenerated after making the revisions (See attached).

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

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

Content Uniformity and Dissolution Acceptance Limit Program

VALIDATION PROTOCOL
Version 2.0

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PROTOCOL

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FORMS

- 1 LOAD AND RUN PROGRAM
- 2 PRIMARY WINDOW NAVIGATION
& INPUT ERROR CHECKS
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- 4 PROGRAM STRATEGY & SAS CODE VERIFICATION
- 5 TEST DATA AGREEMENT
- 6 PROBLEM/REQUEST REPORT

PROTOCOL

PURPOSE:

Version 2 of a program that generates content uniformity and dissolution acceptance limits (CuDAL) will be conducted to verify its functionality and reliability in generating acceptance limit tables based on user input.

OVERVIEW:

As part of the International Conference on Harmonization (ICH) effort, the USP has revised general chapter <905>, Uniformity of Dosage Units. The revised, harmonized general chapter Uniformity of Dosage Units <905> printed in *United States Pharmacopeia* 28-NF 23 (1) will take affect in 2007. The final revised version is a result of many discussions as well as several evaluations and recommendations by the PhRMA CMC Statistics Expert Team (2, 3, 4). Bergum (5) published a method for constructing acceptance limits that relates the acceptance criteria directly to multiple stage tests such as the USP content uniformity and dissolution tests. Bergum and Utter (6, 7) discussed several statistical techniques for evaluating content uniformity. Bergum (8) wrote a SASTM program that implements his method. The program performs the calculations and generates acceptance limit tables. Since the USP test for content uniformity has been revised, new mathematical calculations for content uniformity and a revised SASTM program were developed to generate acceptance limit tables. No changes were needed for dissolution.

The acceptance limits are defined to provide, with a stated confidence level $(1 - \alpha)100\%$, that there is at least a stated probability (P) that a sample taken from a batch would pass the content uniformity test. For example, one can make the statement that, with 95% confidence, there is at least a 95% probability that future samples from the batch will pass the USP content uniformity test. For the revised USP test, these tables change with the confidence level $(1 - \alpha)$, the probability bound (P), the sample size (n) and the target content per dosage unit. Confidence levels as well as values for P are typically 50%, 90%, or 95%. A PDA Technical Report (9) suggests the use of a 90% confidence level to provide 95% coverage. A 50% confidence level can be considered a “best estimate” of the coverage.

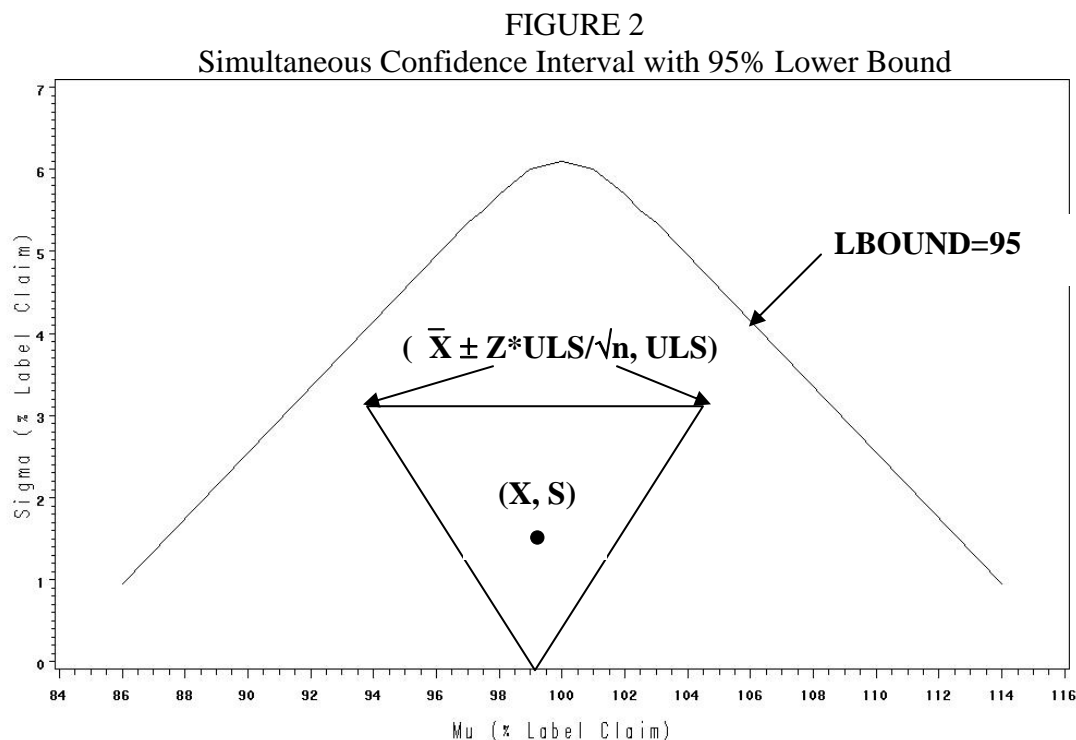
Constructing Acceptance Limits

Assume that the content uniformity test results follow a normal distribution with mean μ and standard deviation σ . Sigma (σ) is the standard deviation of a single observation. For a given value of μ and a given value of σ , a lower bound (LBOUND) can be determined (See Appendix E for detailed calculations).

The LBOUND can be used to develop acceptance limits. This is done by first constructing a simultaneous confidence interval for μ and σ from the data. If a 90% confidence interval is constructed for μ and σ and the entire interval is below the 95% LBOUND, then with 90% confidence, at least 95% of the samples tested would pass the USP test.

Construction of the confidence intervals depends on the sampling plan used to collect the samples. There are two sampling plans that are generally used when testing blends or final product. In the first plan (Sampling Plan 1), a single test result is obtained from each location sampled. For example, in a blending step, a single test result would be obtained from each of a number of different locations within the blender. In a drum, a single test result might be obtained from the different locations within the drum or from each of a number of different drums. For final tablets, a single tablet may be tested from various time points throughout the tableting run. In the second plan (Sampling Plan 2), more than one test result is obtained from each of the sampled locations. For example, during the tableting operation, if a cup is placed under the tablet press at specific time points during the tableting run, several of the tablets from each cup sample would be tested for content uniformity. Sampling Plan 2 allows for estimation of between location and within location variability.

For Sampling Plan 1, the sample mean and sample standard deviation estimate the population parameters μ and σ . A simultaneous confidence interval for μ and σ is given in Lindgren (10). The interval and the 95% LBOUND are displayed in Figure 2 where ULS is the upper confidence limit for σ and Z is a standard normal critical value.



Once the confidence interval is constructed, it must fall completely below the specified LBOUND. An acceptance limit table can be generated by finding the largest sample standard deviation for a fixed sample mean such that the resulting confidence interval remains below the pre-specified LBOUND. Note that the only two points to evaluate on the triangle are the two points with the maximum value of sigma.

CuDAL is a set of programs written by James Bergum in SAS™ that can be used to evaluate content uniformity and dissolution data against the current USP XXIII tests. The program will generate an acceptance limit table for content uniformity and/or dissolution that can be applied when using two specific 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 a specific sample result. 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 value of P and C are provided by the user.

DESCRIPTION OF SYSTEM SOFTWARE:

CuDAL was written using SAS™. The program consists of seven files. CuDAL.SAS is the file that contains the file location and is used to launch the program. There are four files that perform the calculations and generate SAS output (CuDAL.SAS, CUSP1.SAS, CUSP2.SAS, DISP1.SAS, and DISP2.SAS). Each file is a Macro written in SAS™. A hardcopy of these programs is given in Appendix A. There are two files (cudal.sas7bcat and Files.sas.org) that provide the graphical user interface (GUI) for user input and navigation of the program. The user interface was written by Saritha Aleti. The windows displayed for user input during the execution of the program are listed in Appendix B. If an input error is made by the user, an error window is displayed. The software was designed to run on any IBM or compatible PC that has SAS™ 8.02 or later.

DESCRIPTION OF SYSTEM HARDWARE:

CuDAL was written in SAS™ Version 8.02 to run on any IBM or compatible PC that has SAS 8.02 or later on it. There are no additional hardware requirements. The PC's used in the validation of CuDAL will be documented in the validation report.

ASSUMPTIONS, EXCLUSIONS, AND OPERATIONAL LIMITATIONS:

The CuDAL program will operate using the appropriate PC hardware and software. There are no operational limits that have been identified at the time of this validation. Since SAS™ is an accepted vendor supplied software package, validation of the SAS™ program itself is not necessary.

The PC's used in the CuDAL validation are considered validated with respect to mice, keyboards, printers, monitors, and diskette drives.

TEST OBJECTIVES/REQUIREMENTS

This testing ensures that the system meets the needs of the business users as listed below:

- User can successfully open the CuDAL.sas.
- User can successfully edit CuDAL to provide location of other required files.
- User can successfully submit CuDAL.sas and obtain initial graphic user interface (GUI) window.
- User can successfully exit SAS from initial window.
- User can successfully enter the application.
- Program can provide a window that lists tests (content uniformity and dissolution) and sampling plan choices (sampling plan 1 or 2).
- User can successfully select any of the four test/sampling plan combinations.
- Program can provide appropriate window for each selected test/sampling plan.
- User can successfully input required numeric analysis information for each test/sampling plan.
 - Content Uniformity - Sampling Plan 1
 - Sample Size
 - Target
 - Lower Bound
 - Confidence Level
 - Content Uniformity - Sampling Plan 2
 - Number of Locations
 - Number per Location
 - Target
 - Lower Bound
 - Confidence Level
 - Dissolution - Sampling Plan 1
 - Q
 - Sample Size
 - Lower Bound (Numeric)
 - Confidence Level (Numeric)
 - Dissolution - Sampling Plan 2
 - Q
 - Number of Locations

- Number per Location
 - Target
 - Lower Bound
 - Confidence Level
 - Increments for Output Table Between and Within Standard Deviations.
- Program will generate error window if numeric data is not within allowable ranges.
- User can successfully select desired analyses for each selected test/sampling plan.
 - Print Acceptance Limit Table
 - Evaluation of Probability to Pass Acceptance Limit Table
 - Find Lower Bound for specific sample results.
- If a print of the acceptance limit table is selected, the program will output a table:
 - The Sampling Plan 1 table will list means and corresponding CV limits.
 - The Sampling Plan 2 table will provide a range (lower and upper means) for various combinations of within and between location standard deviations.
- If an evaluation of probability to pass the acceptance limit table is selected, the program will successfully provide a window for the user to enter the following required numeric information.
 - Range of Population means and CV's for Sampling Plan 1
 - Range of Population means, Between Location Standard Deviations, and Within Location Standard Deviations for Sampling Plan 2
- If the user requests finding a lower bound for a specific sample result, the program will successfully provide a window for the user to enter the following required information.
 - Sample Mean and CV for Sampling Plan 1
 - Sample Mean, Between Location Standard Deviation, and Within Location Standard Deviation for Sampling Plan 2
- If an evaluation of probability to pass the acceptance limit table is selected, the program will output a table listing the population values that were requested by the user and the probability that sample results will pass the table.
- If the user requests finding a lower bound for a specific sample result, the program will successfully output the sample values that were given by the user and the lower bound probability.
- The program will successfully allow the user to navigate the program.
 - After analysis of a test/sampling plan will return to the initial screen for that chosen combination.
 - Clicking on a Cancel button will return the user to a "higher level" window.
 - The user can successfully return to the test/sampling plan request window or initial opening window by clicking on a cancel button.

VALIDATION PLAN:

The validation team to perform validation of CuDAL consists of the following individuals:

Stan Alton, J&J Pharmaceutical R&D
Myron Diener, Sanofi-Aventis
Yijie Dong, Bristol-Myers Squibb
Brent Harrington, Wyeth Research
David LeBlond, Abbott
James Pazdan, Novartis Pharmaceuticals
Edith Senderak, Merck & Company, Inc.
Merlin Utter, Wyeth Pharmaceuticals
Rowland Yovonie, Hoffmann-La Roche Inc.

CV's from each member of the validation team will be included in the supporting documentation.

There are three validation sub-teams. Each sub-team will have a lead responsible for signing the validation protocol, validation summary report, and appropriate forms as described in the Validation Step section of the protocol.

1) Macro strategy, SASTM code, and Mathematical calculations:

Yijie Dong (Lead)
Stan Alton
James Pazdan
Edith Senderak
Rowland Yovonie

2) Navigation & Window Input Error Checking:

Myron Diener (Lead)

3) Test Data Evaluation and Independent Calculations-

Merlin Utter (Lead)
Brent Harrington
David LeBlond

The validation steps are described below:

VALIDATION STEPS

1) LOAD AND RUN PROGRAM

Each member of the validation team will:

1. Copy the program files (CuDAL.SAS, CUSP1.SAS, CUSP2.SAS, DISP1.SAS, and DISP2.SAS, cudal.sas7bcat, and Files.sas.org) to their computer
2. Modify the file CuDAL.SAS to indicate location of the files on their PC
3. Submit the program CuDAL.SAS
4. Click on “Enter the Application” on the opening window.
5. Select one of the test/sampling plan combinations.
6. Select Y for all three analyses (Print Table, Evaluate Table, and obtain Lower bound for a specific sample result)
7. Use the default values for all numeric inputs.
8. Compare the output to the appropriate expected output found in Appendix C.
9. Fill out Form 1 to verify that the program loaded properly and the appropriate output was generated.

2) NAVIGATION & TEST FOR INPUT ERRORS IN PRIMARY WINDOWS

The Navigation & Error Checking Sub-team will insure that the program allows the user to navigate through the GUI windows and that the program displays specific error checks. Test data are contained in Appendix D listing the window, requested input, test input, expected response, found response, and a column to record agreement between expected and found response. The Error Checking sub-team will indicate a Y or N in this column after each test indicating whether or not an error window was displayed. Once all error test data checks are complete, Form 2 will be filled out indicating whether or not all error checks passed.

3) VERIFY MATHEMATICAL CALCULATIONS FOR LOWER BOUND

Appendix E contains the mathematical calculations used to calculate the lower bound for each test. Since changes to the dissolution programs only involve user input and not the calculations, only the content uniformity calculations require verification. These calculations will be reviewed by the Macro strategy, SAS code, and Mathematical calculation sub-team for appropriateness & accuracy. Form 3 will be filled out indicating that these calculations were reviewed and are considered correct.

4) **VERIFY PROGRAM STRATEGY AND SAS CODE**

The program will be reviewed by the Macro strategy, SAS™ code, and Mathematical calculation sub team to verify that the strategy is correct, the code implements the strategy correctly, and that the mathematical calculations are implemented correctly. A complete description of the SAS™ programs is given in Appendix F. Since the only changes to the dissolution programs involved user input and not the calculations, only the content uniformity calculations require verification. Form 4 will be filled out to indicate that each macro has been reviewed for strategy, correct code, and mathematical lower bound implementation.

5) **RUN TEST DATA SETS:**

The test data sets are given in Appendix G. The validation team will compare two sets of acceptance limit table results. For content uniformity, the first set of results will be obtained by running the CuDAL program using the specified input values given in the test data set. The second set of results will be obtained by performing an independent calculation of the acceptance limit table result. This calculation will be performed using a software package other than SAS. The validation member performing these calculations will provide software and program details used to perform the calculations. The validation team member performing this part of the validation will fill in the final three columns in the test data table indicating the CuDAL program result, independent calculation result, and whether or not both calculations agree with one another. Results should agree after rounding to the number of digits given in the CuDAL result. For dissolution, independent calculations are not required since the calculations have not changed since version 1. However, Appendix G contains two dissolution tables (sampling plan1 & 2) generated using version 1. These tables will be compared to the dissolution tables generated by version 2.

CRITERIA FOR ACCEPTANCE:

Forms 1- 5 are all signed indicating that the program loaded and ran successfully, input errors return error windows, the mathematical calculations for the lower bound is correct, the strategy used is appropriate, the SAS™ code is correct, and the test data expected result agreed with both the CuDAL output from the validation members own run and the result from the independent calculation.

It will be the responsibility of the validation team leads to determine what impact any problems encountered, either singularly or in total, will have on this validation. The decision to continue or terminate this validation will be made by the validation team leads.

For ultimate acceptance, the program should perform as described without any failure that would compromise the user's confidence in the reliability of this program.

ERROR RESOLUTION:

Errors (discrepancies in results versus expected performance) detected during testing will be recorded on a Problem/Request Report form. A request for error resolution will be transmitted to the programmer (James Bergum). The validation team leads will evaluate and approve/accept all error resolutions received from the programmer.

DOCUMENTATION:

Once validation is done, the following documentation will be placed on a Recordable CD for distribution:

- 1) Version 2 Programs
- 2) Version 2 Validation protocol
- 3) Version 2 Validation report
- 4) Version 1 Validation report

Any additional supporting documentation will be kept by James Bergum.

RESPONSIBILITIES AND AUTHORITY:

Validation protocol preparation: James Bergum

Approval of validation protocol: Validation Sub-Team Leads

Execution of testing procedures: Validation Sub-Team Leads

Evaluation of validation study results: Validation Sub-Team Leads

Preparation of validation study report: James Bergum

Approval of validation study report: Validation Sub-Team Leads

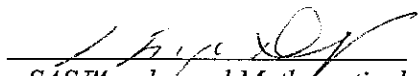
PROTOCOL CHANGES:

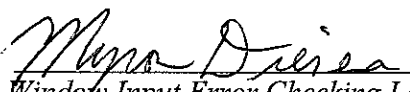
Any changes or revisions of the protocol, and reasons for them, will be documented, dated, and signed by the validation team and will be retained as amendments to the protocol.


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5. Bergum, J.S. (1990), Constructing Acceptance Limits for Multiple Stage Tests. *Drug Development and Industrial Pharmacy*, 16(14), 2153-2166.
6. Bergum, J.S. and Utter M.L. (2000), Process Validation. *Encyclopedia of Biopharmaceutical Statistics*, 422-439.
7. 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, 667-697.
8. J. S. Bergum’s SAS™ Programs, *Content Uniformity and Dissolution Acceptance Limits (CUDAL)*, version: 1.0, validation completed 02/11/02.
9. Blend Uniformity Analysis: Validation and in-process testing. Technical Report No. 25. PDA J Pharm Sci Tech (suppl.) 51 (1997)
10. Lindgren, B.W. *Statistical Theory* New York: Macmillan (1968).
11. Graybill, F.A., Wang, C.M. Confidence Intervals on Nonnegative Linear Combination of Variances, *J American Statistical Association* 75:869-873 (1980)

PROTOCOL APPROVAL

Name:  Date: 5/10/07
Macro strategy, SASTM code, and Mathematical calculations Lead

Name  Date: 5/10/07
Navigation & Window Input Error Checking Lead

Name  Date: 05/10/2007
Test Data Evaluation and Independent Calculations Lead

APPENDIX A PROGRAMS

CuDAL.SAS

```
1. ***** LIBRARY FOR THE APPLICATION*****;
2. /* deleting the macro variables */
3. data vars;
      i. set sashelp.vmacro;
4. run;
5. data _null_;
      i. set vars;
      ii. if scope='GLOBAL' and name ^= 'SYSODSPATH' then
      iii. call execute('%syndel '||trim(left(name))|| ';' );
6. run;

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

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

CUSP1.SAS

```
1. %MACRO CUSP1(A1CUSP1=,
2. A2CUSP1=,
3. A3CUSP1=);
4. %LET D=0.1;

5. data _null_;
6. set mcusp1;
7. CALL SYMPUT( "NUMBER", PUT(LNUMBER, 4.0));
8. CALL SYMPUT( "T", PUT(LT, 5.1));
9. CALL SYMPUT( "LBOUND", PUT(LLBOUND, 4.1));
10. CALL SYMPUT( "CILEVEL", PUT(LCILEVEL, 4.1));
11. run;

12. %IF %UPCASE(&A2CUSP1)=Y %THEN %DO;
13. data _null_;
14. set ev1;
15. CALL SYMPUT( "ULOW", PUT(LULOW, 4.0));
16. CALL SYMPUT( "UHIGH", PUT(LUHIGH, 4.0));
17. CALL SYMPUT( "UINCRE", PUT(LUINCRE, 4.0));
18. CALL SYMPUT( "UDIV", PUT(LUDIV, 4.0));
19. CALL SYMPUT( "CVLOW", PUT(LCVLOW, 4.0));
20. CALL SYMPUT( "CVHIGH", PUT(LCVHIGH, 4.0));
21. CALL SYMPUT( "CVINCRE", PUT(LCVINCRE, 4.0));
22. CALL SYMPUT( "CVDIV", PUT(LCVDIV, 4.0));
23. RUN;
24. %END;
25. %ELSE %IF %UPCASE(&A2CUSP1)=N %THEN %DO;
26. data _null_;
27. CALL SYMPUT( "ULOW", PUT(950, 4.0));
28. CALL SYMPUT( "UHIGH", PUT(1000, 4.0));
29. CALL SYMPUT( "UINCRE", PUT(50, 4.0));
30. CALL SYMPUT( "UDIV", PUT(10, 4.0));
31. CALL SYMPUT( "CVLOW", PUT(10, 4.0));
32. CALL SYMPUT( "CVHIGH", PUT(40, 4.0));
33. CALL SYMPUT( "CVINCRE", PUT(30, 4.0));
34. CALL SYMPUT( "CVDIV", PUT(10, 4.0));
35. RUN;
36. %END;

37. %IF %UPCASE(&A3CUSP1)=Y %THEN %DO;
38. data _null_;
39. set smpl;
40. CALL SYMPUT( "MEAN", PUT(LMEAN, 6.3));
41. CALL SYMPUT( "CV", PUT(LCV, 6.3));
42. CALL SYMPUT( "LCV", PUT(LCV, 6.3));

43. run;
44. %END;
45. %IF %UPCASE(&A3CUSP1)=N %THEN %DO;
46. data _null_;
47. CALL SYMPUT( "MEAN", PUT(100, 6.3));
48. CALL SYMPUT( "CV", PUT(4, 6.3));
49. CALL SYMPUT( "LCV", PUT(4, 6.3));
```

```

50.      run;
51.      %END;

52.      %macro clcalc;
53.      TARGET = &T;
54.      mu=LLU;
55.      n1=10;
56.      n2=30;
57.      k1=2.4;
58.      k2=2.0;
59.      L1=15;
60.      L2=25;
61.      if TARGET LE 101.5 then E =101.5;
62.      else E = TARGET;

63.      z1=(E-mu)*sqrt(n1)/sigma;
64.      z2=(98.5-mu)*sqrt(n1)/sigma;
65.      chil=probchi((n1-1)*L1**2/(k1*sigma)**2, n1-1);
66.      int1=(probnorm(z1)-probnorm(z2))*chil;
67.      t=1;
68.      h=0.05;
69.      int2=0;
70.      do x=E to (E+15-h) by h;
71.      x1=(x-mu)*sqrt(n1)/sigma;
72.      x2=(x+h-mu)*sqrt(n1)/sigma;
73.      chi2=(n1-1)*(E+15-x-h/2)**2/(k1*sigma)**2;
74.      int2=int2+(probnorm(x2)-probnorm(x1))*probchi(chi2, n1-1);
75.      end;

76.      int3=0;
77.      do x=(98.5-15) to (98.5-h) by h;
78.      x1=(x-mu)*sqrt(n1)/sigma;
79.      x2=(x+h-mu)*sqrt(n1)/sigma;
80.      chi3=(n1-1)*(15-98.5+x+h/2)**2/(k1*sigma)**2;
81.      int3=int3+(probnorm(x2)-probnorm(x1))*probchi(chi3, n1-1);
82.      end;

83.      P1=int1+int2+int3;

84.      zz1=(E-mu)*sqrt(n2)/sigma;
85.      zz2=(98.5-mu)*sqrt(n2)/sigma;
86.      cchil=probchi((n2-1)*L1**2/(k2*sigma)**2, n2-1);
87.      iint1=(probnorm(zz1)-probnorm(zz2))*cchil;
88.      iint2=0;
89.      do xx=E to (E+15-h) by h;
90.      xx1=(xx-mu)*sqrt(n2)/sigma;
91.      xx2=(xx+h-mu)*sqrt(n2)/sigma;
92.      cchi2=(n2-1)*(E+15-xx-h/2)**2/(k2*sigma)**2;
93.      iint2=iint2+(probnorm(xx2)-probnorm(xx1))*probchi(cchi2,
n2-1);
94.      end;

95.      iint3=0;
96.      do xx=(98.5-15) to (98.5-h) by h;
97.      xx1=(xx-mu)*sqrt(n2)/sigma;
98.      xx2=(xx+h-mu)*sqrt(n2)/sigma;

```



```

99.      cchi3=(n2-1)*(15-98.5+xx+h/2)**2/(k2*sigma)**2;
100.     iint3=iint3+(probnorm(xx2)-probnorm(xx1))*probchi(cchi3,
      n2-1);
101.     end;

102.     P2a=iint1+iint2+iint3;

103.     zzz1=(123.125-mu)/sigma;
104.     if TARGET LE 101.5 then zzz2=(101.5-24.625-mu)/sigma;
105.     else zzz2 = (TARGET-24.625-mu)/sigma;

106.     P2b=(probnorm(zzz1)-probnorm(zzz2))*30;

107.     P2=max(0, P2a+P2b-1);

108.     overlbd=max(P1, P2);

109.     mu=ULU;
110.     n1=10;
111.     n2=30;
112.     k1=2.4;
113.     k2=2.0;
114.     L1=15;
115.     L2=25;

116.     z1=(E-mu)*sqrt(n1)/sigma;
117.     z2=(98.5-mu)*sqrt(n1)/sigma;
118.     chi1=probchi((n1-1)*L1**2/(k1*sigma)**2, n1-1);
119.     int1=(probnorm(z1)-probnorm(z2))*chi1;
120.     t=1;
121.     h=0.05;
122.     int2=0;
123.     do x=E to (E+15-h) by h;
124.     x1=(x-mu)*sqrt(n1)/sigma;
125.     x2=(x+h-mu)*sqrt(n1)/sigma;
126.     chi2=(n1-1)*(E+15-x-h/2)**2/(k1*sigma)**2;
127.     int2=int2+(probnorm(x2)-probnorm(x1))*probchi(chi2, n1-1);
128.     end;

129.     int3=0;
130.     do x=(98.5-15) to (98.5-h) by h;
131.     x1=(x-mu)*sqrt(n1)/sigma;
132.     x2=(x+h-mu)*sqrt(n1)/sigma;
133.     chi3=(n1-1)*(15-98.5+x+h/2)**2/(k1*sigma)**2;
134.     int3=int3+(probnorm(x2)-probnorm(x1))*probchi(chi3, n1-1);
135.     end;

136.     P1=int1+int2+int3;

137.     zz1=(E-mu)*sqrt(n2)/sigma;
138.     zz2=(98.5-mu)*sqrt(n2)/sigma;
139.     cchi1=probchi((n2-1)*L1**2/(k2*sigma)**2, n2-1);
140.     iint1=(probnorm(zz1)-probnorm(zz2))*cchi1;
141.     iint2=0;
142.     do xx=E to (E+15-h) by h;

```

```

143.     xx1=(xx-mu)*sqrt(n2)/sigma;
144.     xx2=(xx+h-mu)*sqrt(n2)/sigma;
145.     cchi2=(n2-1)*(E+15-xx-h/2)**2/(k2*sigma)**2;
146.     iint2=iint2+(probnorm(xx2)-probnorm(xx1))*probchi(cchi2,
n2-1);
147.     end;

148.     iint3=0;
149.     do xx=(98.5-15) to (98.5-h) by h;
150.     xx1=(xx-mu)*sqrt(n2)/sigma;
151.     xx2=(xx+h-mu)*sqrt(n2)/sigma;
152.     cchi3=(n2-1)*(15-98.5+xx+h/2)**2/(k2*sigma)**2;
153.     iint3=iint3+(probnorm(xx2)-probnorm(xx1))*probchi(cchi3,
n2-1);
154.     end;

155.     P2a=iint1+iint2+iint3;

156.     zzz1=(123.125-mu)/sigma;
157.     if TARGET LE 101.5 then zzz2=(101.5-24.625-mu)/sigma;
158.     else zzz2 = (TARGET-24.625-mu)/sigma;

159.     P2b=(probnorm(zzz1)-probnorm(zzz2))**30;

160.     P2=max(0, P2a+P2b-1);

161.     overubd=max(P1, P2);

162.     OVERBD = MIN(OVERLBD, OVERUBD);
163.     %mend clcalc;

164.     %MACRO CALCUSP1;
165.     DATA TAB;
166.     LABEL OVERBD = 'OVERALL LOWER BOUND'
- MEAN = 'SAMPLE MEAN(%CLAIM)';
167.     D=&D;
168.     Z = PROBIT((1 + SQRT(&CILEVEL / 100)) / 2);
169.     N = &NUMBER;
170.     CHI = CINV(1 - SQRT(&CILEVEL / 100),N - 1);
171.     SDOLD = 0;
172.     STARTSD = 0.01;
173.     DO MEAN = 85.1 TO 114.9 BY D;
174.     BEGIN = STARTSD;
175.     DO SAMPSD = BEGIN TO 7.8 BY 0.001;
176.     SIGMA = SQRT((N - 1) * SAMPSD * SAMPSD / CHI);
177.     LLU = MEAN - Z *SIGMA / SQRT(N);
178.     ULU = MEAN + Z * SIGMA / SQRT(N);
179.     %clcalc
180.     IF OVERBD < &LBOUND/100 AND SAMPSD <= 0.0101 THEN DO;
181.     CV = 0; OUTPUT; SAMPSD = 20.0; GOTO NEXTT; END;
182.     IF OVERBD < &LBOUND/100 THEN DO;
183.     SAMPSD = SAMPSD - 0.001;
184.     IF SAMPSD < SDOLD THEN DO;
- STARTM = MEAN;
- GOTO UPPER;
i. END;
185.     SDOLD = SAMPSD;

```

```

186.     STARTSD = SAMPSD;
187.     CV = 100 * SAMPSD / MEAN;
      - OUTPUT;
      - SAMPSD = 20.0;
      - END;
188.     NEXTT:
189.     END;
190.     END;
191.     GOTO FINISH;
192.     UPPER:
          i. STARTSD = 0.01;

193.     DO MEAN = 114.9 TO STARTM BY -D;
194.     DO SAMPSD = STARTSD TO 7.8 BY 0.001;
195.     SIGMA = SQRT((N - 1) * SAMPSD * SAMPSD / CHI);
196.     LLU = MEAN - Z * SIGMA / SQRT(N);
197.     ULU = MEAN + Z * SIGMA / SQRT(N);
198.     %c1calc
199.     IF OVERBD < &LBOUND/100 AND SAMPSD <= 0.0101 THEN DO;
200.     CV = 0; OUTPUT; SAMPSD = 20.0; GOTO NEXTB; END;
201.     IF OVERBD < &LBOUND/100 THEN DO;
202.     SAMPSD = SAMPSD - 0.001;
203.     STARTSD = SAMPSD;
204.     CV = 100 * SAMPSD / MEAN;
      - OUTPUT;
      - SAMPSD = 20.0;
      - END;
205.     NEXTB:
206.     END;
207.     END;
208.     FINISH:
209.     KEEP CV MEAN;
210.     PROC SORT DATA=TAB; BY MEAN;
211.     DATA
212.     ONE(RENAME = (MEAN = X1 CV = CV1))
213.     TWO(RENAME = (MEAN = X2 CV = CV2))
214.     THREE(RENAME = (MEAN = X3 CV = CV3))
215.     FOUR(RENAME = (MEAN = X4 CV = CV4))
216.     FIVE(RENAME = (MEAN = X5 CV = CV5))
217.     SIX(RENAME = (MEAN = X6 CV = CV6));
218.     SET TAB;
219.     IF MEAN <= 90.05 THEN OUTPUT ONE;
220.     IF 90.05 < MEAN <= 95.05 THEN OUTPUT TWO;
221.     IF 95.05 < MEAN <= 100.05 THEN OUTPUT THREE;
222.     IF 100.05 < MEAN <= 105.05 THEN OUTPUT FOUR;
223.     IF 105.05 < MEAN <= 110.05 THEN OUTPUT FIVE;
224.     IF 110.05 < MEAN <= 115.0 THEN OUTPUT SIX;
225.     DATA SEVEN;
226.     MERGE ONE TWO THREE FOUR FIVE SIX;
227.     RUN;
228.     %MEND CALCUSP1;

229.     %MACRO PRTCUSP1;
230.     OPTIONS MISSING = ' ' NODATE NONUMBER;
231.     OPTIONS LS=132;
232.     PROC PRINT DATA=SEVEN SPLIT = '*';
233.     FORMAT CV1 CV2 CV3 CV4 CV5 CV6 5.2;

```

```

234. LABEL
- X1 = ' MEAN*(% CLAIM)'
- X2 = ' MEAN*(% CLAIM)'
- X3 = ' MEAN*(% CLAIM)'
- X4 = ' MEAN*(% CLAIM)'
- X5 = ' MEAN*(% CLAIM)'
- X6 = ' MEAN*(% CLAIM)'
- CV1 = 'CV*(%)'
- CV2 = 'CV*(%)'
- CV3 = 'CV*(%)'
- CV4 = 'CV*(%)'
- CV5 = 'CV*(%)'
- CV6 = 'CV*(%)';
235. VAR CV1 X2 CV2 X3 CV3 X4 CV4 X5 CV5 X6 CV6;
236. ID X1;
237. TITLE1 "ACCEPTANCE LIMITS FOR CONTENT UNIFORMITY(N=&NUMBER,
TARGET = &T)";
238. TITLE2 "SAMPLING PLAN 1";
239. TITLE3 "(MEETING LIMITS GUARANTEES, WITH &CILEVEL.%
ASSURANCE, THAT AT LEAST";
240. TITLE4 "&LBOUND.% OF SAMPLES TESTED FOR CONTENT UNIFORMITY
WILL PASS THE USP TEST)";
241. %MEND PRTCUSP1;

242. %MACRO EVCUSP1;

243. DATA TAB;
244. SET SEVEN;

245. %MACRO DSCUSP1;
246. %DO I = 1 %TO 6;
247. DATA DATA&I;
- SET TAB;
- STD = X&I * CV&I / 100; RENAME X&I = X;
- KEEP X&I STD;
248. %END;

249. %MEND DSCUSP1;

250. %DSCUSP1

251. DATA ONE;
252. SET DATA1 DATA2 DATA3 DATA4 DATA5 DATA6;
253. N = &NUMBER;
254. RUN;

255. %MACRO SIGCUSP1;

256. %DO CV = &CVLOW %TO &CVHIGH %BY &CVINCRE;
257. %DO U = &ULOW %TO &UHIGH %BY &UINCRE;

- DATA SAVE;
i. SET ONE END = LAST;
ii. U = &U / &UDIV;
iii. CV = &CV / &CVDIV;
iv. SIGMA = U * CV / 100;
v. PMEAN = PROBNORM((x - U) * SQRT(N) / SIGMA)

```

```

-   PROBNORM((LAG(X) - U) * SQRT(N) / SIGMA);
    i. AVEHT = (STD + LAG(STD)) / 2;
    ii. PSTD = PROBCHI((N - 1) * AVEHT * AVEHT
        1. / (SIGMA * SIGMA), N - 1);
    iii. PT = PMEAN * PSTD ;
    iv. PTRAP + PT;
    v. IF LAST THEN OUTPUT;
-   RUN;

258.   PROC APPEND BASE = SAVEALL DATA = SAVE;

-   %END;
259.   %END;

260.   %MEND SIGCUSP1;

261.   %SIGCUSP1

262.   OPTIONS NODATE NONUMBER;
263.   PROC PRINT DATA = SAVEALL split = '*';
264.   label ptrap = 'PROBABILITY*OF*PASSING';
265.   VAR CV PTRAP;
266.   ID U;
267.   TITLE1 "ACCEPTANCE LIMIT TABLE FOR CONTENT
UNIFORMITY(N=&NUMBER)";
268.   TITLE2 "SAMPLING PLAN 1";
269.   TITLE3 'DETERMINE PROBABILITY OF PASSING ACCEPTANCE LIMIT
TABLE';
270.   TITLE4 "CONFIDENCE LEVEL = &CILEVEL AND LOWER BOUND =
&LBOUND";
271.   RUN;
272.   %MEND EVCUSP1;

273.   %MACRO SMPCUSP1;

274.   %let TARGET = &T;
275.   DATA TAB;
276.   LABEL OVERBD = 'OVERALL LOWER BOUND'
-   MEAN = 'SAMPLE MEAN(%CLAIM)';
277.   CILEVEL = &CILEVEL;
278.   Z = PROBIT((1 + SQRT(&CILEVEL / 100)) / 2);
279.   N = &NUMBER;
280.   CHI = CINV(1 - SQRT(&CILEVEL / 100), N - 1);
281.   MEAN = &MEAN;
282.   CV = &LCV;
283.   SAMPSD= &MEAN * CV/100;
284.   SIGMA = SQRT((N - 1) * SAMPSD * SAMPSD / CHI);
285.   LLU = MEAN - Z * SIGMA / SQRT(N);
286.   ULU = MEAN + Z * SIGMA / SQRT(N);
287.   %clcalc

288.   OPTIONS NODATE NONUMBER;
289.   PROC PRINT SPLIT = '*';
290.   LABEL SAMPSD = 'SAMPLE*STD DEV*(% CLAIM)'
-   MEAN = 'SAMPLE* MEAN*(% CLAIM)'
-   OVERBD = 'LOWER BOUND';
291.   ID MEAN;

```

```

292.      VAR SAMPSD CV OVERBD;
293.      TITLE1 "ACCEPTANCE LIMIT TABLE FOR CONTENT
      UNIFORMITY(N=&NUMBER)";
294.      TITLE2 "SAMPLING PLAN 1";
295.      TITLE3 'DETERMINE PROBABILITY OF FUTURE SAMPLES PASSING THE
      USP TEST';
296.      TITLE4 "WITH &CILEVEL ASSURANCE FOR GIVEN SAMPLE MEAN AND
      CV";
297.      run;
298.      %MEND SMPCUSP1;

299.      %MACRO ANACUSP1;
300.      %IF %UPCASE(&A1CUSP1)=Y OR %UPCASE(&A2CUSP1)=Y %THEN %DO;
301.      %CALCUSP1;
302.      %END;
303.      %IF %UPCASE(&A1CUSP1)=Y %THEN %DO;
304.      %PRTCUSP1;
305.      %END;
306.      %IF %UPCASE(&A2CUSP1)=Y %THEN %DO;
307.      %EVCUSP1;
308.      PROC DATASETS LIBRARY = WORK;
309.      DELETE SAVEALL;
310.      quit;
311.      %END;
312.      %IF %UPCASE(&A3CUSP1)=Y %THEN %DO;
313.      %SMPCUSP1;
314.      %END;
315.      %MEND ANACUSP1;

316.      %ANACUSP1

317.      RUN;
318.      %MEND CUSP1;
319.      %CUSP1

```

CUSP2.SAS

```
1. %MACRO CUSP2(A1CUSP2=,
2. A2CUSP2=,
3. A3CUSP2=);
4. %LET D1=0.10;

5. OPTIONS NODATE NONUMBER;

6. data _null_;
7. set mcusp2;
8. CALL SYMPUT( "LOC", PUT(LLOC, 4.0));
9. CALL SYMPUT( "NUM", PUT(LNUM, 4.0));
10. CALL SYMPUT( "T", PUT(LT, 5.1));
11. CALL SYMPUT( "LBOUND", PUT(LLBOUND, 4.1));
12. CALL SYMPUT( "CILEVEL", PUT(LCILEVEL, 4.1));
13. run;

14. %IF %UPCASE(&A2CUSP2)=Y %THEN %DO;
15. data _null_;
16. set ev2;
17. CALL SYMPUT( "ULOW", PUT(LULOW, 4.0));
18. CALL SYMPUT( "UHIGH", PUT(LUHIGH, 4.0));
19. CALL SYMPUT( "UINCRE", PUT(LUINCRE, 4.0));
20. CALL SYMPUT( "UDIV", PUT(LUDIV, 4.0));
21. CALL SYMPUT( "SELOW", PUT(LSELOW, 4.0));
22. CALL SYMPUT( "SEHIGH", PUT(LSEHIGH, 4.0));
23. CALL SYMPUT( "SEINCRE", PUT(LSEINCRE, 4.0));
24. CALL SYMPUT( "SEDIV", PUT(LSEDIV, 4.0));
25. CALL SYMPUT( "SMLow", PUT(LSMLow, 4.0));
26. CALL SYMPUT( "SMHIGH", PUT(LSMHIGH, 4.0));
27. CALL SYMPUT( "SMINCRE", PUT(LSMINCRE, 4.0));
28. CALL SYMPUT( "SMDIV", PUT(LSMDIV, 4.0));
29. RUN;
30. %END;
31. %ELSE %IF %UPCASE(&A2CUSP2)=N %THEN %DO;
32. data _null_;
33. CALL SYMPUT( "ULOW", PUT(950, 4.0));
34. CALL SYMPUT( "UHIGH", PUT(1000, 4.0));
35. CALL SYMPUT( "UINCRE", PUT(50, 4.0));
36. CALL SYMPUT( "UDIV", PUT(10, 4.0));
37. CALL SYMPUT( "SELOW", PUT(22, 4.0));
38. CALL SYMPUT( "SEHIGH", PUT(22, 4.0));
39. CALL SYMPUT( "SEINCRE", PUT(10, 4.0));
40. CALL SYMPUT( "SEDIV", PUT(10, 4.0));
41. CALL SYMPUT( "SMLow", PUT(22, 4.0));
42. CALL SYMPUT( "SMHIGH", PUT(22, 4.0));
43. CALL SYMPUT( "SMINCRE", PUT(10, 4.0));
44. CALL SYMPUT( "SMDIV", PUT(10, 4.0));
45. RUN;
46. %END;

47. %IF %UPCASE(&A3CUSP2)=Y %THEN %DO;
48. data _null_;
```

```

49.      set smp2;
50.      CALL SYMPUT( "MEAN", PUT(LMEAN, 6.3));
51.      CALL SYMPUT( "SE", PUT(LSE, 6.3));
52.      CALL SYMPUT( "SM", PUT(LSM, 6.3));
53.      run;
54.      %END;
55.      %ELSE %IF %UPCASE(&A3CUSP2)=N %THEN %DO;
56.      data _null_;
57.      CALL SYMPUT( "MEAN", PUT(100, 6.3));
58.      CALL SYMPUT( "SE", PUT(2.2, 6.3));
59.      CALL SYMPUT( "SM", PUT(2.46, 6.3));
60.      run;
61.      %END;
62.      %macro cullu;
63.      LLU = MEAN - Z * SQRT(MVAR / N);
64.      TARGET = &T;
65.      mu=LLU;
66.      n1=10;
67.      n2=30;
68.      k1=2.4;
69.      k2=2.0;
70.      L1=15;
71.      L2=25;
72.      if TARGET LE 101.5 then E =101.5;
73.      else E = TARGET;

74.      z1=(E-mu)*sqrt(n1)/sigma;
75.      z2=(98.5-mu)*sqrt(n1)/sigma;
76.      chil=probchi((n1-1)*L1**2/(k1*sigma)**2, n1-1);
77.      int1=(probnorm(z1)-probnorm(z2))*chil;
78.      t=1;
79.      h=0.05;
80.      int2=0;
81.      do x=E to (E+15-h) by h;
82.      x1=(x-mu)*sqrt(n1)/sigma;
83.      x2=(x+h-mu)*sqrt(n1)/sigma;
84.      chi2=(n1-1)*(E+15-x-h/2)**2/(k1*sigma)**2;
85.      int2=int2+(probnorm(x2)-probnorm(x1))*probchi(chi2, n1-1);
86.      end;

87.      int3=0;
88.      do x=(98.5-15) to (98.5-h) by h;
89.      x1=(x-mu)*sqrt(n1)/sigma;
90.      x2=(x+h-mu)*sqrt(n1)/sigma;
91.      chi3=(n1-1)*(15-98.5+x+h/2)**2/(k1*sigma)**2;
92.      int3=int3+(probnorm(x2)-probnorm(x1))*probchi(chi3, n1-1);
93.      end;

94.      P1=int1+int2+int3;

95.      zz1=(E-mu)*sqrt(n2)/sigma;
96.      zz2=(98.5-mu)*sqrt(n2)/sigma;
97.      cchil=probchi((n2-1)*L1**2/(k2*sigma)**2, n2-1);
98.      iint1=(probnorm(zz1)-probnorm(zz2))*cchil;
99.      iint2=0;
100.     do xx=E to (E+15-h) by h;

```



```

101.      xx1=(xx-mu)*sqrt(n2)/sigma;
102.      xx2=(xx+h-mu)*sqrt(n2)/sigma;
103.      cchi2=(n2-1)*(E+15-xx-h/2)**2/(k2*sigma)**2;
104.      iint2=iint2+(probnorm(xx2)-probnorm(xx1))*probchi(cchi2,
n2-1);
105.      end;

106.      iint3=0;
107.      do xx=(98.5-15) to (98.5-h) by h;
108.      xx1=(xx-mu)*sqrt(n2)/sigma;
109.      xx2=(xx+h-mu)*sqrt(n2)/sigma;
110.      cchi3=(n2-1)*(15-98.5+xx+h/2)**2/(k2*sigma)**2;
111.      iint3=iint3+(probnorm(xx2)-probnorm(xx1))*probchi(cchi3,
n2-1);
112.      end;

113.      P2a=iint1+iint2+iint3;

114.      zzz1=(123.125-mu)/sigma;
115.      if TARGET LE 101.5 then zzz2=(101.5-24.625-mu)/sigma;
116.      else zzz2 = (TARGET-24.625-mu)/sigma;

117.      P2b=(probnorm(zzz1)-probnorm(zzz2))*30;

118.      P2=max(0, P2a+P2b-1);

119.      overbdl=max(P1, P2);

120.      %MEND cullu;

121.      %MACRO cuulu;
122.      ULU = MEAN + Z * SQRT(MVAR / N);
123.      TARGET = &T;
124.      mu=ULU;
125.      n1=10;
126.      n2=30;
127.      k1=2.4;
128.      k2=2.0;
129.      L1=15;
130.      L2=25;
131.      if TARGET LE 101.5 then E =101.5;
132.      else E = TARGET;

133.      z1=(E-mu)*sqrt(n1)/sigma;
134.      z2=(98.5-mu)*sqrt(n1)/sigma;
135.      chil=probchi((n1-1)*L1**2/(k1*sigma)**2, n1-1);
136.      int1=(probnorm(z1)-probnorm(z2))*chil;
137.      t=1;
138.      h=0.05;
139.      int2=0;
140.      do x=E to (E+15-h) by h;
141.      x1=(x-mu)*sqrt(n1)/sigma;
142.      x2=(x+h-mu)*sqrt(n1)/sigma;
143.      chi2=(n1-1)*(E+15-x-h/2)**2/(k1*sigma)**2;
144.      int2=int2+(probnorm(x2)-probnorm(x1))*probchi(chi2, n1-1);
145.      end;

```

```

146.     int3=0;
147.     do x=(98.5-15) to (98.5-h) by h;
148.     x1=(x-mu)*sqrt(n1)/sigma;
149.     x2=(x+h-mu)*sqrt(n1)/sigma;
150.     chi3=(n1-1)*(15-98.5+x+h/2)**2/(k1*sigma)**2;
151.     int3=int3+(probnorm(x2)-probnorm(x1))*probchi(chi3, n1-1);
152.     end;

153.     P1=int1+int2+int3;

154.     zz1=(E-mu)*sqrt(n2)/sigma;
155.     zz2=(98.5-mu)*sqrt(n2)/sigma;
156.     cchi1=probchi((n2-1)*L1**2/(k2*sigma)**2, n2-1);
157.     iint1=(probnorm(zz1)-probnorm(zz2))*cchi1;
158.     iint2=0;
159.     do xx=E to (E+15-h) by h;
160.     xx1=(xx-mu)*sqrt(n2)/sigma;
161.     xx2=(xx+h-mu)*sqrt(n2)/sigma;
162.     cchi2=(n2-1)*(E+15-xx-h/2)**2/(k2*sigma)**2;
163.     iint2=iint2+(probnorm(xx2)-probnorm(xx1))*probchi(cchi2,
n2-1);
164.     end;

165.     iint3=0;
166.     do xx=(98.5-15) to (98.5-h) by h;
167.     xx1=(xx-mu)*sqrt(n2)/sigma;
168.     xx2=(xx+h-mu)*sqrt(n2)/sigma;
169.     cchi3=(n2-1)*(15-98.5+xx+h/2)**2/(k2*sigma)**2;
170.     iint3=iint3+(probnorm(xx2)-probnorm(xx1))*probchi(cchi3,
n2-1);
171.     end;

172.     P2a=iint1+iint2+iint3;

173.     zzz1=(123.125-mu)/sigma;
174.     if TARGET LE 101.5 then zzz2=(101.5-24.625-mu)/sigma;
175.     else zzz2 = (TARGET-24.625-mu)/sigma;

176.     P2b=(probnorm(zzz1)-probnorm(zzz2))**30;

177.     P2=max(0, P2a+P2b-1);

178.     overbdu=max(P1, P2);

179.     %mend cuulu;

180.     %MACRO CALCUSP2;
181.     DATA TABC;
182.     D=&D1;
183.     Z = PROBIT((1 + SQRT(&CILEVEL/100))/2);
184.     NN = &NUM;
185.     L = &LOC;
186.     N = NN*L;
187.     CALL SYMPUT("TOT",PUT(N, 5.0));
188.     CHIERR = CINV(1 - SQRT(&CILEVEL / 100), L*(NN - 1));

```

```

189.      CHILOC = CINV(1 - SQRT(&CILEVEL / 100),L-1);
190.      SEBOUND = 9.2;
191.      SMLIM = 9.2;
192.      NEXTL = 84.9;
193.      NEXTU = 115.1;
194.      DO SE = D TO SEBOUND BY D;
195.      MEANL = NEXTL;
196.      MEANU = NEXTU;
197.      SMBOUND = SMLIM;
198.      SE2 = SE * SE;
199.      H2 = L * (NN - 1) / CHIERR - 1;
200.      SEC = ((1 - 1/NN)*H2*SE2)**2;
201.      DO SM = D TO SMBOUND BY D;
202.      IF MEANL = . THEN GOTO OVER;
203.      SL2 = SM * SM * NN;
204.      SL2UB = (L - 1) * SL2 / CHILOC;
205.      H1 = (L - 1) / CHILOC - 1;
206.      FIRST = ((1 / NN)*H1*SL2)**2;
207.      PTEST = (1 / NN) * SL2 + (1 - 1/NN) * SE2;
208.      VAR = PTEST + SQRT(FIRST + SEC);
209.      MVAR = SL2UB;
210.      SIGMA = SQRT(VAR);
211.      DO MEAN = MEANL - D TO 115.5 BY D;
212.      %cullu
213.      IF OVERBDL > &LBOUND/100 THEN DO;
214.      MEANL = MEAN;
215.      GOTO UPPER;
216.      END;
217.      END;
218.      MEANL = .;
219.      MEANU = .;
220.      IF SE=D THEN DO;
221.      SMLIM = SM - D;
222.      OUTPUT;
223.      SM=10;
224.      GOTO OVER;
          1. END;
225.      IF SM=D THEN DO; SE = 10; GOTO OVER; END;
226.      GOTO SKIP;
227.      UPPER:

228.      DO MEAN = MEANU + D TO 84.9 BY -D;
229.      %cuulu
230.      IF OVERBDU > &LBOUND/100 THEN DO;
231.      MEANU = MEAN;
232.      GOTO OUT;
233.      END;
234.      END;
235.      OUT:
236.      IF MEANU <= MEANL OR MEAN <= MEANL THEN DO;
237.      MEANL = .;
238.      MEANU = .;
239.      IF SE=D THEN DO;
240.      SMLIM = SM - D;
241.      OUTPUT;
242.      SM=10;
243.      GOTO OVER;

```

```

244.      END;
245.      IF SM=D THEN DO; SE = 10; GOTO OVER; END;
246.      END;

247.      SKIP: OUTPUT;
248.      IF SM = D THEN DO;
249.          NEXTL = MEANL;
250.          NEXTU = MEANU;
251.      a. END;
252.      OVER:
253.      END;
254.      KEEP N NN L D MEAN SE SM MEANL MEANU OVERBDL OVERBDU;
255.      data tabc;
256.      set tabc;
257.      if SE = 10 or SM = 10 then delete;
258.      run;
259.      PROC SORT DATA=TABC; BY SE SM;run;

260.      %MEND CALCUSP2;

261.      %MACRO PRTCUSP2;
262.      options ls=132;
263.      PROC TRANSPOSE DATA = TABC OUT = LDAT PREFIX = L;
264.      VAR MEANL;
265.      BY SE;

266.      PROC TRANSPOSE DATA = TABC OUT = UDAT PREFIX = U;
267.      VAR MEANU;
268.      BY SE;

269.      DATA together;
270.      MERGE LDAT UDAT;
271.      BY SE;
272.      proc sort data=together; by se;
273.      data miss;
274.      l1=.; u1=.;
275.      l2=.; u2=.;
276.      l3=.; u3=.;
277.      l4=.; u4=.;
278.      l5=.; u5=.;
279.      l6=.; u6=.;
280.      l7=.; u7=.;
281.      l8=.; u8=.;
282.      l9=.; u9=.;
283.      l10=.; u10=.;
284.      l11=.; u11=.;
285.      l12=.; u12=.;
286.      l13=.; u13=.;
287.      l14=.; u14=.;
288.      l15=.; u15=.;
289.      l16=.; u16=.;
290.      l17=.; u17=.;
291.      l18=.; u18=.;
292.      l19=.; u19=.;
293.      l20=.; u20=.;
294.      l21=.; u21=.;

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```
295.      122=. ; u22=. ;
296.      123=. ; u23=. ;
297.      124=. ; u24=. ;
298.      125=. ; u25=. ;
299.      126=. ; u26=. ;
300.      127=. ; u27=. ;
301.      128=. ; u28=. ;
302.      129=. ; u29=. ;
303.      130=. ; u30=. ;
304.      131=. ; u31=. ;
305.      132=. ; u32=. ;
306.      133=. ; u33=. ;
307.      134=. ; u34=. ;
308.      135=. ; u35=. ;
309.      136=. ; u36=. ;
310.      137=. ; u37=. ;
311.      138=. ; u38=. ;
312.      139=. ; u39=. ;
313.      140=. ; u40=. ;
314.      141=. ; u41=. ;
315.      142=. ; u42=. ;
316.      143=. ; u43=. ;
317.      144=. ; u44=. ;
318.      145=. ; u45=. ;
319.      146=. ; u46=. ;
320.      147=. ; u47=. ;
321.      148=. ; u48=. ;
322.      149=. ; u49=. ;
323.      150=. ; u50=. ;
324.      151=. ; u51=. ;
325.      152=. ; u52=. ;
326.      153=. ; u53=. ;
327.      154=. ; u54=. ;
328.      155=. ; u55=. ;
329.      156=. ; u56=. ;
330.      157=. ; u57=. ;
331.      158=. ; u58=. ;
332.      159=. ; u59=. ;
333.      160=. ; u60=. ;
334.      161=. ; u61=. ;
335.      162=. ; u62=. ;
336.      163=. ; u63=. ;
337.      164=. ; u64=. ;
338.      165=. ; u65=. ;
339.      166=. ; u66=. ;
340.      167=. ; u67=. ;
341.      168=. ; u68=. ;
342.      169=. ; u69=. ;
343.      170=. ; u70=. ;
344.      171=. ; u71=. ;
345.      172=. ; u72=. ;
346.      data all;
347.      merge miss together;
348.      DATA _NULL_;
349.      SET ALL;
350.      IF L1 EQ . THEN RETURN;
351.      FILE PRINT HEADER = TOP;
```

```

352.      PUT @1 SE 3.1 +1
353.      (L1 U1 L2 U2 L3 U3 L4 U4 L5 U5 L6 U6 L7 U7 L8 U8 L9 U9)
354.      (5.1 +1 5.1 +2);
355.      RETURN;
356.      TOP: PUT / @9 '0.1' +10 '0.2' +10 '0.3' +10 '0.4' +10 '0.5'
+10
          i. '0.6' +10 '0.7' +10 '0.8' +10 '0.9' //
          ii. @1 'SE' @7 'LL' @12 'UL' @20 'LL' @25 'UL' @33 'LL'
          iii. @38 'UL' @46 'LL' @51 'UL' @59 'LL' @64 'UL' @72 'LL'
          iv. @77 'UL' @85 'LL' @90 'UL' @98 'LL' @103 'UL'
          v. @111 'LL' @116 'UL' //;
357.      RETURN;
358.      TITLE1 "ACCEPTANCE LIMITS FOR CONTENT UNIFORMITY";
359.      TITLE2 'SAMPLING PLAN 2';
360.      TITLE3 "TARGET=&T, LOWER BOUND = &LBOUND, CONFIDENCE LEVEL
= &CILEVEL";
361.      TITLE4 'TABLE ENTRIES ARE LOWER(LL) AND UPPER(UL) LIMITS ON
THE MEAN';
362.      TITLE5 "OF &TOT ASSAYS-&NUM ASSAYS AT EACH OF &LOC
DIFFERENT LOCATIONS";
363.      TITLE6 'SE IS THE POOLED WITHIN LOCATION STANDARD
DEVIATION';
364.      TITLE7 'STANDARD DEVIATIONS AND MEANS ARE EXPRESSED IN %
CLAIM';
365.      TITLE9 'STANDARD DEVIATION OF LOCATION MEANS';

366.      DATA _NULL_;
367.      SET ALL;
368.      IF L10 EQ . THEN RETURN;
369.      FILE PRINT HEADER = TOP;
370.      PUT @1 SE 3.1 +1
371.      (L10 U10 L11 U11 L12 U12 L13 U13 L14 U14
372.      L15 U15 L16 U16 L17 U17 L18 U18)
373.      (5.1 +1 5.1 +2);
374.      RETURN;
375.      TOP: PUT / @9 '1.0' +10 '1.1' +10 '1.2' +10 '1.3' +10 '1.4'
+10
          i. '1.5' +10 '1.6' +10 '1.7' +10 '1.8' //
          ii. @1 'SE' @7 'LL' @12 'UL' @20 'LL' @25 'UL' @33 'LL'
          iii. @38 'UL' @46 'LL' @51 'UL' @59 'LL' @64 'UL' @72 'LL'
          iv. @77 'UL' @85 'LL' @90 'UL' @98 'LL' @103 'UL'
          v. @111 'LL' @116 'UL' //;
376.      RETURN;
377.      DATA _NULL_;
378.      SET ALL;
379.      IF L19 EQ . THEN RETURN;
380.      FILE PRINT HEADER = TOP;
381.      PUT @1 SE 3.1 +1
382.      (L19 U19 L20 U20 L21 U21 L22 U22 L23 U23
383.      L24 U24 L25 U25 L26 U26 L27 U27)
384.      (5.1 +1 5.1 +2);
385.      RETURN;
386.      TOP: PUT / @9 '1.9' +10 '2.0' +10 '2.1' +10 '2.2' +10 '2.3'
+10
          i. '2.4' +10 '2.5' +10 '2.6' +10 '2.7' //
          ii. @1 'SE' @7 'LL' @12 'UL' @20 'LL' @25 'UL' @33 'LL'
          iii. @38 'UL' @46 'LL' @51 'UL' @59 'LL' @64 'UL' @72 'LL'

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        iv. @77 'UL' @85 'LL' @90 'UL' @98 'LL' @103 'UL'
           v. @111 'LL' @116 'UL' //;
387. RETURN;
388. DATA _NULL_;
389. SET ALL;
390. IF L28 = . THEN RETURN;
391. FILE PRINT HEADER = TOP;
392. PUT @1 SE 3.1 +1
393. (L28 U28 L29 U29 L30 U30 L31 U31 L32 U32
394. L33 U33 L34 U34 L35 U35 L36 U36)
395. (5.1 +1 5.1 +2);
396. RETURN;
397. TOP: PUT / @9 '2.8' +10 '2.9' +10 '3.0' +10 '3.1' +10 '3.2'
+10
        i. '3.3' +10 '3.4' +10 '3.5' +10 '3.6' //
        ii. @1 'SE' @7 'LL' @12 'UL' @20 'LL' @25 'UL' @33 'LL'
        iii. @38 'UL' @46 'LL' @51 'UL' @59 'LL' @64 'UL' @72 'LL'
        iv. @77 'UL' @85 'LL' @90 'UL' @98 'LL' @103 'UL'
        v. @111 'LL' @116 'UL' //;
398. RETURN;
399. DATA _NULL_;
400. SET ALL;
401. IF L37 EQ . THEN RETURN;
402. FILE PRINT HEADER = TOP;
403. PUT @1 SE 3.1 +1
404. (L37 U37 L38 U38 L39 U39 L40 U40 L41 U41
405. L42 U42 L43 U43 L44 U44 L45 U45)
406. (5.1 +1 5.1 +2);
407. RETURN;
408. TOP: PUT / @9 '3.7' +10 '3.8' +10 '3.9' +10 '4.0' +10 '4.1'
+10
        i. '4.2' +10 '4.3' +10 '4.4' +10 '4.5' //
        ii. @1 'SE' @7 'LL' @12 'UL' @20 'LL' @25 'UL' @33 'LL'
        iii. @38 'UL' @46 'LL' @51 'UL' @59 'LL' @64 'UL' @72 'LL'
        iv. @77 'UL' @85 'LL' @90 'UL' @98 'LL' @103 'UL'
        v. @111 'LL' @116 'UL' //;
409. RETURN;
410. DATA _NULL_;
411. SET ALL;
412. IF L46 EQ . THEN RETURN;
413. FILE PRINT HEADER = TOP;
414. PUT @1 SE 3.1 +1
415. (L46 U46 L47 U47 L48 U48 L49 U49 L50 U50
416. L51 U51 L52 U52 L53 U53 L54 U54)
417. (5.1 +1 5.1 +2);
418. RETURN;
419. TOP: PUT / @9 '4.6' +10 '4.7' +10 '4.8' +10 '4.9' +10 '5.0'
+10
        i. '5.1' +10 '5.2' +10 '5.3' +10 '5.4' //
        ii. @1 'SE' @7 'LL' @12 'UL' @20 'LL' @25 'UL' @33 'LL'
        iii. @38 'UL' @46 'LL' @51 'UL' @59 'LL' @64 'UL' @72 'LL'
        iv. @77 'UL' @85 'LL' @90 'UL' @98 'LL' @103 'UL'
        v. @111 'LL' @116 'UL' //;
420. RETURN;
421. DATA _NULL_;
422. SET ALL;
423. IF L55 EQ . THEN RETURN;

```

```

424. FILE PRINT HEADER = TOP;
425. PUT @1 SE 3.1 +1
426. (L55 U55 L56 U56 L57 U57 L58 U58 L59 U59
427. L60 U60 L61 U61 L62 U62 L63 U63)
428. (5.1 +1 5.1 +2);
429. RETURN;
430. TOP: PUT / @9 '5.5' +10 '5.6' +10 '5.7' +10 '5.8' +10 '5.9'
+10
      i. '6.0' +10 '6.1' +10 '6.2' +10 '6.3' //
      ii. @1 'SE' @7 'LL' @12 'UL' @20 'LL' @25 'UL' @33 'LL'
      iii. @38 'UL' @46 'LL' @51 'UL' @59 'LL' @64 'UL' @72 'LL'
      iv. @77 'UL' @85 'LL' @90 'UL' @98 'LL' @103 'UL'
      v. @111 'LL' @116 'UL' //;
431. RETURN;
432. DATA _NULL_;
433. SET ALL;
434. IF L64 EQ . THEN RETURN;
435. FILE PRINT HEADER = TOP;
436. PUT @1 SE 3.1 +1
437. (L64 U64 L65 U65 L66 U66 L67 U67 L68 U68
438. L69 U69 L70 U70 L71 U71 L72 U72)
439. (5.1 +1 5.1 +2);
440. RETURN;
441. TOP: PUT / @9 '6.4' +10 '6.5' +10 '6.6' +10 '6.7' +10 '6.8'
+10
      i. '6.9' +10 '7.0' +10 '7.1' +10 '7.2' //
      ii. @1 'SE' @7 'LL' @12 'UL' @20 'LL' @25 'UL' @33 'LL'
      iii. @38 'UL' @46 'LL' @51 'UL' @59 'LL' @64 'UL' @72 'LL'
      iv. @77 'UL' @85 'LL' @90 'UL' @98 'LL' @103 'UL'
      v. @111 'LL' @116 'UL' //;
442. RETURN;

443. run;
444. %MEND PRTCUSP2;

445. %MACRO EVCUSP2;

446. %MACRO SIGCUSP2;
447. %calcusp2
448. %DO U = &ULOW %TO &UHIGH %BY &UINCRE;
449. %DO SIGSE = &SELOW %TO &SEHIGH %BY &SEINCRE;
a. %DO SIGSM = &SMLOW %TO &SMHIGH %BY &SMINCRE;

450. DATA SAVE2;
451. SET TABC END = LAST;
452. U = &U / &UDIV;
453. D = &D1;
454. SIGSE = &SIGSE / &SEDIV;
455. SIGSM = &SIGSM / &SMDIV;
456. SIGSM2 = SIGSM * SIGSM;
457. EXPSE2 = SIGSE * SIGSE;
458. EXPSM2 = EXPSE2 + NN * SIGSM * SIGSM;
459. PMEAN = PROBNORM((MEANU - U) * SQRT((N) / EXPSM2));
a. PROBNORM((MEANL - U) * SQRT((N) / EXPSM2));
460. PSE = PROBCHI(L * (NN - 1) * SE * SE / EXPSE2, L * (NN - 1))

```



```

a. PROBCHI(L * (NN - 1) * (SE - D) * (SE - D) /
b. EXPSE2, L * (NN - 1));
461. PSM = PROBCHI((L - 1) * NN * SM * SM / EXPSM2, L - 1)
a. PROBCHI((L - 1) * NN * (SM - D) * (SM - D) /
b. EXPSM2, L - 1);
462. P = PMEAN * PSE * PSM;
463. PSUM + P;
464. IF LAST THEN OUTPUT;
465. RUN;
466. PROC APPEND BASE = SAVES2E DATA = SAVE2;
467. RUN;

a. %END;
468. %END;
469. %END;

470. %MEND SIGCUSP2;

471. %SIGCUSP2

472. PROC PRINT DATA = SAVES2E split = '*';
473. label U = 'MEAN'
a. SIGSE = 'WITHIN LOCATION*STD DEV'
b. SIGSM = 'BETWEEN LOCATION* STD DEV'
c. PSUM = 'PROBABILITY*OF*PASSING';
474. VAR U SIGSE SIGSM PSUM;
475. TITLE1 "ACCEPTANCE LIMITS FOR CONTENT UNIFORMITY";
476. TITLE2 'SAMPLING PLAN 2';
477. TITLE3 "PROBABILITY OF PASSING ACCEPTANCE LIMIT TABLE";
478. TITLE4 "WITH &NUM ASSAYS AT EACH OF &LOC LOCATIONS";
479. TITLE5 "CONFIDENCE LEVEL = &CILEVEL & LOWER BOUND =
&LBOUND";
480. RUN;
481. %MEND EVCUSP2;

482. %MACRO SMPCUSP2;

483. DATA TAB;
484. Z = PROBIT((1 + SQRT(&CILEVEL/100))/2);
485. NN = &NUM;
486. L = &LOC;
487. N = NN*L;
488. SE = &SE;
489. SM = &SM;
490. MEAN = &MEAN;
491. CILEVEL = &CILEVEL;
492. CHIERR = CINV(1 - SQRT(&CILEVEL / 100), L*(NN - 1));
493. CHILOC = CINV(1 - SQRT(&CILEVEL / 100), L-1);
494. SE2 = SE * SE;
495. H2 = L * (NN - 1) / CHIERR - 1;
496. SEC = ((1 - 1/NN)*H2*SE2)**2;
497. SL2 = SM * SM * NN;
498. SL2UB = (L - 1) * SL2 / CHILOC;
499. H1 = (L - 1) / CHILOC - 1;
500. FIRST = ((1 / NN)*H1*SL2)**2;
501. PTEST = (1 / NN) * SL2 + (1 - 1/NN) * SE2;
502. VAR = PTEST + SQRT(FIRST + SEC);

```

```

503.      MVAR = SL2UB;
504.      SIGMA = SQRT(VAR);
505.      %cullu
506.      %cuulu
507.      OVERBD = MIN(OVERBDU, OVERBDL);
508.      KEEP SE MEAN SM OVERBD;
509.      PROC PRINT SPLIT='*';
510.      LABEL SE = 'SAMPLE*WITHIN LOCATION*STD DEV'
      a. MEAN = 'SAMPLE*MEAN'
      b. SM = 'SAMPLE*BETWEEN LOCATION*STD DEV'
      c. OVERBD = 'LOWER BOUND';
511.      ID MEAN;
512.      VAR SE SM OVERBD;
513.      TITLE1 "ACCEPTANCE LIMITS FOR CONTENT UNIFORMITY";
514.      TITLE2 "SAMPLING PLAN 2 (&LOC LOCATIONS, &NUM PER
LOCATION)";
515.      TITLE3 "PROPORTION OF FUTURE SAMPLES PASSING THE USP TEST";
516.      TITLE4 "WITH &CILEVEL.% ASSURANCE";
517.      TITLE5 'FOR GIVEN SAMPLE MEAN, WITHIN AND BETWEEN LOCATION
STD DEV';
518.      RUN;
519.      %MEND SMPCUSP2;

520.      %MACRO ANACUSP2;

521.      %IF %UPCASE(&A1CUSP2)=Y %THEN %DO;
522.      %CALCUSP2;
523.      %PRTCUSP2;
524.      %END;
525.      %IF %UPCASE(&A2CUSP2)=Y %THEN %DO;
526.      %EVCUSP2;
527.      PROC DATASETS LIBRARY=WORK;
528.      DELETE SAVES2E;
529.      %END;
530.      %IF %UPCASE(&A3CUSP2)=Y %THEN %DO;
531.      %SMPCUSP2;
532.      %END;
533.      %MEND ANACUSP2;

534.      %ANACUSP2

535.      RUN;
536.      %MEND CUSP2;
537.      %CUSP2

```

DISP1.SAS

```
1. %MACRO DISP1(A1DISP1=,
2. A2DISP1=,
3. A3DISP1=);

4. data _null_;
5. set mdisp1;
6. CALL SYMPUT( "Q", PUT(LQ, 4.1));
7. CALL SYMPUT( "NUMBER", PUT(LNUMBER, 4.0));
8. CALL SYMPUT( "LBOUND", PUT(LLBOUND, 4.1));
9. CALL SYMPUT( "CILEVEL", PUT(LCILEVEL, 4.1));
10. run;

11. %IF %UPCASE(&A2DISP1)=Y %THEN %DO;
12. data _null_;
13. set ev1;
14. CALL SYMPUT( "ULOW", PUT(LULOW, 4.0));
15. CALL SYMPUT( "UHIGH", PUT(LUHIGH, 4.0));
16. CALL SYMPUT( "UINCRE", PUT(LUINCRE, 4.0));
17. CALL SYMPUT( "UDIV", PUT(LUDIV, 4.0));
18. CALL SYMPUT( "CVLOW", PUT(LCVLOW, 4.0));
19. CALL SYMPUT( "CVHIGH", PUT(LCVHIGH, 4.0));
20. CALL SYMPUT( "CVINCRE", PUT(LCVINCRE, 4.0));
21. CALL SYMPUT( "CVDIV", PUT(LCVDIV, 4.0));
22. RUN;
23. %END;
24. %ELSE %IF %UPCASE(&A2DISP1)=N %THEN %DO;
25. data _null_;
26. CALL SYMPUT( "ULOW", PUT(950, 4.0));
27. CALL SYMPUT( "UHIGH", PUT(1000, 4.0));
28. CALL SYMPUT( "UINCRE", PUT(50, 4.0));
29. CALL SYMPUT( "UDIV", PUT(10, 4.0));
30. CALL SYMPUT( "CVLOW", PUT(10, 4.0));
31. CALL SYMPUT( "CVHIGH", PUT(40, 4.0));
32. CALL SYMPUT( "CVINCRE", PUT(30, 4.0));
33. CALL SYMPUT( "CVDIV", PUT(10, 4.0));
34. RUN;
35. %END;

36. %IF %UPCASE(&A3DISP1)=Y %THEN %DO;
37. data _null_;
38. set smp1;
39. CALL SYMPUT( "MEAN", PUT(LMEAN, 6.2));
40. CALL SYMPUT( "CV", PUT(LCV, 6.2));
41. CALL SYMPUT( "LCV", PUT(LCV, 6.2));
42. run;
43. %END;
44. %ELSE %IF %UPCASE(&A3DISP1)=N %THEN %DO;
45. data _null_;
46. CALL SYMPUT( "MEAN", PUT(100, 6.2));
47. CALL SYMPUT( "CV", PUT(4, 6.2));
48. CALL SYMPUT( "LCV", PUT(4, 6.2));
49. run;
50. %END;
```

```

51.      %MACRO COMPUTE;
52.      F1 = (1 - PROBNORM((5 - LLU)/SIGMA)) ** 6;
53.      SN2 = SQRT(12);
54.      PM2 = PROBNORM (SN2 * -LLU / SIGMA);
55.      PB2 = 1 - PROBNORM ((-15 - LLU) / SIGMA);
56.      F2 = PB2 ** 12 - PM2;
57.      SN3 = SQRT(24);
58.      PM3 = PROBNORM (SN3 * -LLU / SIGMA);
59.      P2 = PROBNORM ((-15 - LLU) / SIGMA) - PROBNORM ((-25 - LLU)
/ SIGMA);
60.      P3 = 1 - PROBNORM ((-15 - LLU) / SIGMA);
61.      F3 = P3**24 + 24*P2*P3**23 + 276*P2*P2*P3**22 - PM3;
62.      OVERBD = MAX(F1, F2, F3);
63.      %mend compute;
64.      %MACRO CALDISP1;
65.      DATA D1ONE;
66.      Q = &Q;
67.      LIM = 100 - Q;
68.      N = &NUMBER;
69.      D=0.2;
70.      Z = PROBIT(SQRT(&CILEVEL / 100));
71.      CHI = CINV(1 - SQRT(&CILEVEL / 100),N - 1);
72.      STARTSD = 0.002;
73.      DO MEANADJ = D TO LIM BY D;
74.      BEGIN = STARTSD;
75.      DO SAMPSD = BEGIN TO 60.0 BY 0.001;
76.      SIGMA = SQRT((N - 1) * SAMPSD * SAMPSD / CHI);
77.      LLU = MEANADJ - Z *SIGMA / SQRT(N);
78.      %COMPUTE
79.      IF OVERBD < &LBOUND/100 AND SAMPSD <= 0.00201 then do;
80.      CV = 0; OUTPUT; SAMPLSD = 65.0; GOTO NEXT; END;
81.      IF OVERBD < &LBOUND/100 THEN DO;
82.      SAMPSD = SAMPSD - 0.001;
83.      STARTSD = SAMPSD;
84.      MEAN = MEANADJ + Q;
85.      CV = 100 * SAMPSD / MEAN;
      a. OUTPUT;
      b. SAMPSD = 65.0;
      c. END;
86.      NEXT;
87.      END;
88.      END;
89.      KEEP CV MEAN ;
90.      PROC SORT DATA=D1ONE; BY MEAN;
91.      DATA
92.      ONE(RENAME = (MEAN = X1 CV = CV1))
93.      TWO(RENAME = (MEAN = X2 CV = CV2))
94.      THREE(RENAME = (MEAN = X3 CV = CV3))
95.      FOUR(RENAME = (MEAN = X4 CV = CV4))
96.      FIVE(RENAME = (MEAN = X5 CV = CV5));
97.      SET D1ONE;
98.      Q = &Q;
99.      LIM = 100 - Q;
100.     IF Q < MEAN <= Q+ LIM/5 + 0.0001 THEN
      OUTPUT ONE;

```

```

101.      IF Q+LIM/5 + 0.0001 < MEAN <= Q+ 2*LIM/5 + 0.0001 THEN
      OUTPUT TWO;
102.      IF Q+2*LIM/5 + 0.0001 < MEAN <= Q+ 3*LIM/5 + 0.0001 THEN
      OUTPUT THREE;
103.      IF Q+3*LIM/5 + 0.0001 < MEAN <= Q+ 4*LIM/5 + 0.0001 THEN
      OUTPUT FOUR;
104.      IF Q+4*LIM/5 + 0.0001 < MEAN <= Q+ LIM + 0.0001 THEN
      OUTPUT FIVE;
105.      DATA D1ALL;
106.      MERGE ONE TWO THREE FOUR FIVE;
107.      RUN;

108.      %MEND CALDISP1;

109.      %MACRO PRTDISP1;
110.      OPTIONS MISSING = ' ' NODATE NONUMBER;
111.      OPTIONS LS=132;
112.      PROC PRINT DATA=D1ALL SPLIT = '*';
113.      FORMAT CV1 CV2 CV3 CV4 CV5 5.2;
114.      LABEL
      a. X1 = ' MEAN*(% CLAIM) '
      b. X2 = ' MEAN*(% CLAIM) '
      c. X3 = ' MEAN*(% CLAIM) '
      d. X4 = ' MEAN*(% CLAIM) '
      e. X5 = ' MEAN*(% CLAIM) '
      f. CV1 = 'CV*(%) '
      g. CV2 = 'CV*(%) '
      h. CV3 = 'CV*(%) '
      i. CV4 = 'CV*(%) '
      j. CV5 = 'CV*(%) ';
115.      VAR CV1 X2 CV2 X3 CV3 X4 CV4 X5 CV5;
116.      ID X1;
117.      TITLE "ACCEPTANCE LIMITS FOR DISSOLUTION (N = &NUMBER, Q =
      &Q) ";
118.      TITLE2 'SAMPLING PLAN 1';
119.      TITLE3 "(MEETING LIMITS GUARANTEES WITH &CILEVEL %
      ASSURANCE, ";
120.      TITLE4 "THAT AT LEAST &LBOUND% OF ALL FUTURE SAMPLES
      TESTED";
121.      TITLE5 'FOR DISSOLUTION WILL PASS THE USP TEST)';
122.      TITLE6 "TABLE ENTRY IS UPPER LIMIT ON CV OF &NUMBER
      DISSOLUTION ASSAYS";
123.      %MEND PRTDISP1;

124.      %MACRO EVDISP1;

125.      DATA DIONE;
126.      SET d1one;
127.      x = mean;
128.      std = x*cv/100;
129.      N = &NUMBER;

130.      %MACRO SIGDISP1;

131.      %DO CV = &CVLOW %TO &CVHIGH %BY &CVINCRE;

```

```

132.      %DO U = &ULOW %TO &UHIGH %BY &UINCRE;

      a. DATA D1SAVE;
          i. SET DIONE END = LAST;
          ii. U = &U / &UDIV;
          iii. CV = &CV / &CVDIV;
          iv. SIGMA = U * CV / 100;
          v. PMEAN = PROBNORM((X - U) * SQRT(N) / SIGMA)
      b. PROBNORM((LAG(X) - U) * SQRT(N) / SIGMA);
          i. AVEHT = (STD + LAG(STD)) / 2;
          ii. PSTD = PROBCHI((N - 1) * AVEHT * AVEHT
              1. / (SIGMA * SIGMA), N - 1);
          iii. PT = PMEAN * PSTD ;
          iv. PTRAP + PT;
          v. IF X > 99.9 THEN DO;
          vi. PMEAN = 1 - PROBNORM((X - U) * SQRT (N) / SIGMA);
          vii. PSTD = PROBCHI((N - 1) * STD * STD
              a. / (SIGMA * SIGMA), N - 1);
          viii. PT = PMEAN * PSTD;
          ix. PTRAP + PT;
          x. END;
          xi. IF LAST THEN OUTPUT;
      c. RUN;

133.      PROC APPEND BASE = D1SAVALL DATA = D1SAVE;

      a. %END;

134.      %END;

135.      %MEND SIGDISP1;

136.      %SIGDISP1

137.      PROC PRINT DATA = D1SAVALL split = '*';
138.      label ptrap = 'PROBABILITY*OF*PASSING';
139.      VAR CV PTRAP;
140.      ID U;
141.      TITLE "ACCEPTANCE LIMITS FOR DISSOLUTION (N = &NUMBER, Q =
          &Q)";
142.      TITLE2 'SAMPLING PLAN 1';
143.      TITLE3 'PROBABILITY OF PASSING ACCEPTANCE LIMIT TABLE';
144.      TITLE4 "CONFIDENCE LEVEL = &CILEVEL AND LOWER BOUND =
          &LBOUND";
145.      RUN;
146.      %MEND EVDISP1;

147.      %MACRO SMPDISP1;

148.      DATA DI1SMP;
149.      LABEL OVERBD = 'OVERALL LOWER BOUND'
      a. MEAN = 'SAMPLE MEAN(%CLAIM)';
150.      Q = &Q;
151.      N = &NUMBER;
152.      CILEVEL = &CILEVEL;
153.      Z = PROBIT(SQRT(&CILEVEL / 100));
154.      N = &NUMBER;
155.      CHI = CINV(1 - SQRT(&CILEVEL / 100), N - 1);

```

```

156.     MEAN = &MEAN;
157.     MEANADJ = MEAN - Q;
158.     CV = &LCV;
159.     SAMPSD= &MEAN * CV/100;
160.     SIGMA = SQRT((N - 1) * SAMPSD * SAMPSD / CHI);
161.     LLU = MEANADJ - Z *SIGMA / SQRT(N);
162.     %COMPUTE
163.     PROC PRINT SPLIT = '*';
164.     LABEL SAMPSD = 'SAMPLE*STD DEV*(% CLAIM)'
      a. MEAN = 'SAMPLE* MEAN*(% CLAIM)'
      b. OVERBD = 'LOWER BOUND';

165.     ID MEAN;
166.     VAR SAMPSD CV OVERBD;
167.     TITLE "ACCEPTANCE LIMITS FOR DISSOLUTION (N = &NUMBER, Q =
      &Q)";
168.     TITLE2 'SAMPLING PLAN 1';
169.     TITLE3 "PROPORTION OF FUTURE SAMPLES PASSING THE USP TEST";
170.     TITLE4 "FOR A GIVEN SAMPLE MEAN AND CV WITH &CILEVEL.%
      ASSURANCE";
171.     run;
172.     %MEND SMPDISP1;

173.     %MACRO ANADISP1;

174.     %IF %UPCASE(&A1DISP1)=Y OR %UPCASE(&A2DISP1)=Y %THEN %DO;
175.     %CALDISP1;
176.     %END;
177.     %IF %UPCASE(&A1DISP1)=Y %THEN %DO;
178.     %PRTDISP1;
179.     %END;
180.     %IF %UPCASE(&A2DISP1)=Y %THEN %DO;
181.     %EVDISP1;
182.     PROC DATASETS LIBRARY = WORK;
183.     DELETE D1SAVALL;
184.     %END;
185.     %IF %UPCASE(&A3DISP1)=Y %THEN %DO;
186.     %SMPDISP1;
187.     %END;
188.     %MEND ANADISP1;

189.     %ANADISP1
190.     RUN;
191.     %MEND DISP1;
192.     %DISP1

```

DISP2.SAS - No Changes or Additions

```
1. %MACRO DISP2(A1DISP2=,
2. A2DISP2=,
3. A3DISP2=);
4. OPTIONS NODATE NONUMBER;

5. data _null_;
6. set mdisp2;
7. CALL SYMPUT( "Q", PUT(LQ, 4.1));
8. CALL SYMPUT( "DSE", PUT(LDSE, 4.2));
9. CALL SYMPUT( "DSM", PUT(LDSM, 4.2));
10. CALL SYMPUT( "LOC", PUT(LLOC, 4.0));
11. CALL SYMPUT( "NUM", PUT(LNUM, 4.0));
12. CALL SYMPUT( "LBOUND", PUT(LLBOUND, 4.1));
13. CALL SYMPUT( "CILEVEL", PUT(LCILEVEL, 4.1));
14. run;

15. %IF %UPCASE(&A2DISP2)=Y %THEN %DO;
16. data _null_;
17. set ev2;
18. CALL SYMPUT( "ULOW", PUT(LULOW, 4.0));
19. CALL SYMPUT( "UHIGH", PUT(LUHIGH, 4.0));
20. CALL SYMPUT( "UINCRE", PUT(LUINCRE, 4.0));
21. CALL SYMPUT( "UDIV", PUT(LUDIV, 4.0));
22. CALL SYMPUT( "SELOW", PUT(LSELOW, 4.0));
23. CALL SYMPUT( "SEHIGH", PUT(LSEHIGH, 4.0));
24. CALL SYMPUT( "SEINCRE", PUT(LSEINCRE, 4.0));
25. CALL SYMPUT( "SEDIV", PUT(LSEDIV, 4.0));
26. CALL SYMPUT( "SMLow", PUT(LSMLow, 4.0));
27. CALL SYMPUT( "SMHIGH", PUT(LSMHIGH, 4.0));
28. CALL SYMPUT( "SMINCRE", PUT(LSMINCRE, 4.0));
29. CALL SYMPUT( "SMDIV", PUT(LSMDIV, 4.0));
30. RUN;
31. %END;
32. %ELSE %IF %UPCASE(&A2DISP2)=N %THEN %DO;
33. data _null_;
34. CALL SYMPUT( "ULOW", PUT(950, 4.0));
35. CALL SYMPUT( "UHIGH", PUT(1000, 4.0));
36. CALL SYMPUT( "UINCRE", PUT(50, 4.0));
37. CALL SYMPUT( "UDIV", PUT(10, 4.0));
38. CALL SYMPUT( "SELOW", PUT(22, 4.0));
39. CALL SYMPUT( "SEHIGH", PUT(22, 4.0));
40. CALL SYMPUT( "SEINCRE", PUT(10, 4.0));
41. CALL SYMPUT( "SEDIV", PUT(10, 4.0));
42. CALL SYMPUT( "SMLow", PUT(22, 4.0));
43. CALL SYMPUT( "SMHIGH", PUT(22, 4.0));
44. CALL SYMPUT( "SMINCRE", PUT(10, 4.0));
45. CALL SYMPUT( "SMDIV", PUT(10, 4.0));
46. RUN;
47. %END;

48. %IF %UPCASE(&A3DISP2)=Y %THEN %DO;
49. data _null_;
```



```

50.      set smp2;
51.      CALL SYMPUT( "MEAN", PUT(LMEAN, 6.3));
52.      CALL SYMPUT( "SE", PUT(LSE, 6.3));
53.      CALL SYMPUT( "SM", PUT(LSM, 6.3));
54.      run;
55.      %END;
56.      %ELSE %IF %UPCASE(&A3DISP2)=N %THEN %DO;
57.      data _null_;
58.      CALL SYMPUT( "MEAN", PUT(100, 6.3));
59.      CALL SYMPUT( "SE", PUT(2.2, 6.3));
60.      CALL SYMPUT( "SM", PUT(2.46, 6.3));
61.      run;
62.      %END;

63.      %MACRO COMPUTE;
64.      F1 = (1 - PROBNORM((5 - LLU)/SIGMA)) ** 6;
65.      SN2 = SQRT(12);
66.      PM2 = PROBNORM (SN2 * -LLU / SIGMA);
67.      PB2 = 1 - PROBNORM ((-LLU - 15) / SIGMA);
68.      F2 = PB2 ** 12 - PM2;
69.      SN3 = SQRT(24);
70.      PM3 = PROBNORM (SN3 * -LLU / SIGMA);
71.      P2 = PROBNORM ((-LLU - 15) / SIGMA) - PROBNORM ((-LLU - 25)
/ SIGMA);
72.      P3 = 1 - PROBNORM ((-LLU - 15) / SIGMA);
73.      F3 = P3**24 + 24*P2*P3**23 + 276*P2*P2*P3**22 - PM3;
74.      OVERBD = MAX(F1, F2, F3);
75.      %mend compute;

76.      %MACRO CALDISP2;
77.      DATA TABD;
78.      DM =0.10;
79.      DSE = &DSE;
80.      DSM = &DSM;
81.      Q = &Q;
82.      LIM = 100 - Q;
83.      NN = &NUM;
84.      L = &LOC;
85.      N = NN*L;
86.      CALL SYMPUT( "TOT", PUT(N, 5.0));
87.      Z = PROBIT(SQRT(&CILEVEL / 100));
88.      CHIERR = CINV(1 - SQRT(&CILEVEL / 100), L*(NN - 1));
89.      CHILOC = CINV(1 - SQRT(&CILEVEL / 100), L-1);
90.      SEBOUND = 60;
91.      SMLIM = 60;
92.      NEXTM = 0.2;
93.      DO SE = DSE TO SEBOUND BY DSE;
94.      MEANL = NEXTM;
95.      SMBOUND = SMLIM;
96.      SE2 = SE * SE;
97.      H2 = L * (NN - 1) / CHIERR - 1;
98.      SEC = ((1 - 1/NN)*H2*SE2)**2;
99.      DO SM = DSM TO SMBOUND BY DSM;
100.     IF MEANL =. THEN GOTO OVER;
101.     SL2 = SM * SM * NN;

```

```

102.     SL2UB = (L - 1) * SL2 / CHILOC;
103.     H1 = (L - 1) / CHILOC - 1;
104.     FIRST = ((1 / NN)*H1*SL2)**2;
105.     PTEST = (1 / NN) * SL2 + (1 - 1/NN) * SE2;
106.     VAR = PTEST + SQRT(FIRST + SEC);
107.     MVAR = SL2UB;
108.     SIGMA = SQRT(VAR);
109.     DO MEANADJ = MEANL TO LIM BY DM;
110.     LLU = MEANADJ - Z *SQRT(MVAR / N);
111.     %COMPUTE
112.     IF OVERBD > &LBOUND/100 THEN DO;
113.     MEANL = MEANADJ;
114.     GOTO SKIP;

                                i.  END;

115.     END;
116.     MEANL = .;
117.     IF SE=DSE THEN DO;
118.     SMLIM = SM - DSM;
119.     MEAN = MEANL + Q;
120.     OUTPUT;
121.     SM = 90;
122.     GOTO OVER;
                                i.  END;
123.     IF SM=DSM THEN DO; SE = 90; GOTO OVER; END;
124.     SKIP:
125.     MEAN = MEANL + Q;
126.     OUTPUT;
127.     IF SM = DSM THEN NEXTM = MEANL;
128.     OVER:
129.     END;
130.     END;
131.     KEEP N NN L MEAN SE SM OVERBD;
132.     PROC SORT DATA=TABD; BY SE SM;

133.     %MEND CALDISP2;

134.     %MACRO PRTDISP2;
135.     options ls=132;

136.     PROC TABULATE DATA=TABD FORMAT=6.2 FORMCHAR='          ';
137.     CLASS SE SM;
138.     FORMAT SE 6.2 SM 6.2;
139.     VAR MEAN;
140.     TABLE SE, SUM*MEAN = ' ' * (SM = ' ')/rts=8;
141.     KEYLABEL SUM = 'STANDARD DEVIATION OF LOCATION MEANS';
142.     TITLE "ACCEPTANCE LIMITS FOR DISSOLUTION (Q = &Q) ";
143.     TITLE2 'SAMPLING PLAN 2';
144.     TITLE3 "LOWER BOUND = &LBOUND, CONFIDENCE LEVEL =
&CILEVEL";
145.     TITLE4 'TABLE ENTRIES ARE LOWER LIMITS ON THE MEAN';
146.     TITLE5 "OF &TOT ASSAYS-&NUM ASSAYS AT EACH OF &LOC
DIFFERENT LOCATIONS";
147.     TITLE6 'SE IS THE POOLED WITHIN LOCATION STANDARD
DEVIATION';
148.     TITLE7 'STANDARD DEVIATIONS AND MEANS ARE EXPRESSED IN %
CLAIM';

```

```

149.      run;

150.      %MEND PRTDISP2;

151.      %MACRO EVDISP2;

152.      %MACRO SIGDISP2;
153.      %CALDISP2
154.      %DO U = &ULOW %TO &UHIGH %BY &UINCRE;
155.      %DO SIGSE = &SELOW %TO &SEHIGH %BY &SEINCRE;
      a. %DO SIGSM = &SMLOW %TO &SMHIGH %BY &SMINCRE;

156.      DATA SAVE2;
157.      SET TABD END = LAST;
158.      U = &U / &UDIV;
159.      DSE = &DSE;
160.      DSM = &DSM;
161.      SIGSE = &SIGSE / &SEDIV;
162.      SIGSM = &SIGSM / &SMDIV;
163.      SIGSM2 = SIGSM * SIGSM;
164.      EXPSE2 = SIGSE * SIGSE;
165.      EXPSM2 = EXPSE2 + NN * SIGSM * SIGSM;
166.      PMEAN = 1 - PROBNORM((MEAN - U) * SQRT((N) / EXPSM2));
167.      PSE = PROBCHI(L * (NN - 1) * SE * SE / EXPSE2, L * (NN - 1))
      a. PROBCHI(L * (NN - 1) * (SE - DSE) * (SE - DSE) /
      b. EXPSE2, L * (NN - 1));
168.      PSM = PROBCHI((L - 1) * NN * SM * SM / EXPSM2, L - 1)
      a. PROBCHI((L - 1) * NN * (SM - DSM) * (SM - DSM) /
      b. EXPSM2, L - 1);
169.      P = PMEAN * PSE * PSM;
170.      PSUM + P;
171.      IF LAST THEN OUTPUT;
172.      RUN;
173.      PROC APPEND BASE = SAVES2E DATA = SAVE2;
174.      RUN;

      a. %END;
175.      %END;
176.      %END;

177.      %MEND SIGDISP2;

178.      %SIGDISP2

179.      PROC PRINT DATA = SAVES2E split = '*';
180.      label U = 'MEAN'
      a. SIGSE = 'WITHIN LOCATION*STD DEV'
      b. SIGSM = 'BETWEEN LOCATION* STD DEV'
      c. PSUM = 'PROBABILITY*OF*PASSING';
181.      VAR U SIGSE SIGSM PSUM;
182.      TITLE1 "ACCEPTANCE LIMITS FOR DISSOLUTION (Q = &Q) ";
183.      TITLE2 'SAMPLING PLAN 2';
184.      TITLE3 "PROBABILITY OF PASSING DISSOLUTION ACCEPTANCE LIMIT
TABLE";
185.      TITLE4 "WITH &NUM ASSAYS AT EACH OF &LOC LOCATIONS";

```

```

186.     TITLE5 "CONFIDENCE LEVEL = &CILEVEL & LOWER BOUND =
        &LBOUND";
187.     RUN;
188.     %MEND EVDISP2;

189.     %MACRO SMPDISP2;

190.     DATA TAB;
191.     Z = PROBIT(SQRT(&CILEVEL/100));
192.     NN = &NUM;
193.     L = &LOC;
194.     N = NN*L;
195.     SE = &SE;
196.     SM = &SM;
197.     MEAN = &MEAN;
198.     Q = &Q;
199.     MEANADJ = MEAN - Q;
200.     CILEVEL = &CILEVEL;
201.     CHIERR = CINV(1 - SQRT(&CILEVEL / 100), L*(NN - 1));
202.     CHILOC = CINV(1 - SQRT(&CILEVEL / 100), L-1);
203.     SE2 = SE * SE;
204.     H2 = L * (NN - 1) / CHIERR - 1;
205.     SEC = ((1 - 1/NN)*H2*SE2)**2;
206.     SL2 = SM * SM * NN;
207.     SL2UB = (L - 1) * SL2 / CHILOC;
208.     H1 = (L - 1) / CHILOC - 1;
209.     FIRST = ((1 / NN)*H1*SL2)**2;
210.     PTEST = (1 / NN) * SL2 + (1 - 1/NN) * SE2;
211.     VAR = PTEST + SQRT(FIRST + SEC);
212.     MVAR = SL2UB;
213.     SIGMA = SQRT(VAR);
214.     LLU = MEANADJ - Z *SQRT(MVAR / N);
215.     %COMPUTE
216.     KEEP SE MEAN SM OVERBD;
217.     PROC PRINT SPLIT='*';
218.     LABEL    SE = 'SAMPLE*WITHIN LOCATION*STD DEV'
a. MEAN = 'SAMPLE*MEAN'
b. SM = 'SAMPLE*BETWEEN LOCATION*STD DEV'
c. OVERBD = 'LOWER BOUND';
219.     ID MEAN;
220.     VAR SE SM OVERBD;
221.     TITLE "ACCEPTANCE LIMITS FOR DISSOLUTION (Q = &Q) ";
222.     TITLE2 "SAMPLING PLAN 2 (&LOC LOCATIONS, &NUM PER
        LOCATION)";
223.     TITLE3 'PROPORTION OF FUTURE SAMPLES PASSING THE USP TEST';
224.     TITLE4 "WITH &CILEVEL.% ASSURANCE";
225.     TITLE5 'GIVEN THE SAMPLE MEAN, WITHIN AND BETWEEN STD DEV';
226.     RUN;
227.     %MEND SMPDISP2;

228.     %MACRO ANADISP2;

229.     %IF %UPCASE(&A1DISP2)=Y %THEN %DO;
230.     %CALDISP2;
231.     %PRTDISP2;
232.     %END;

```

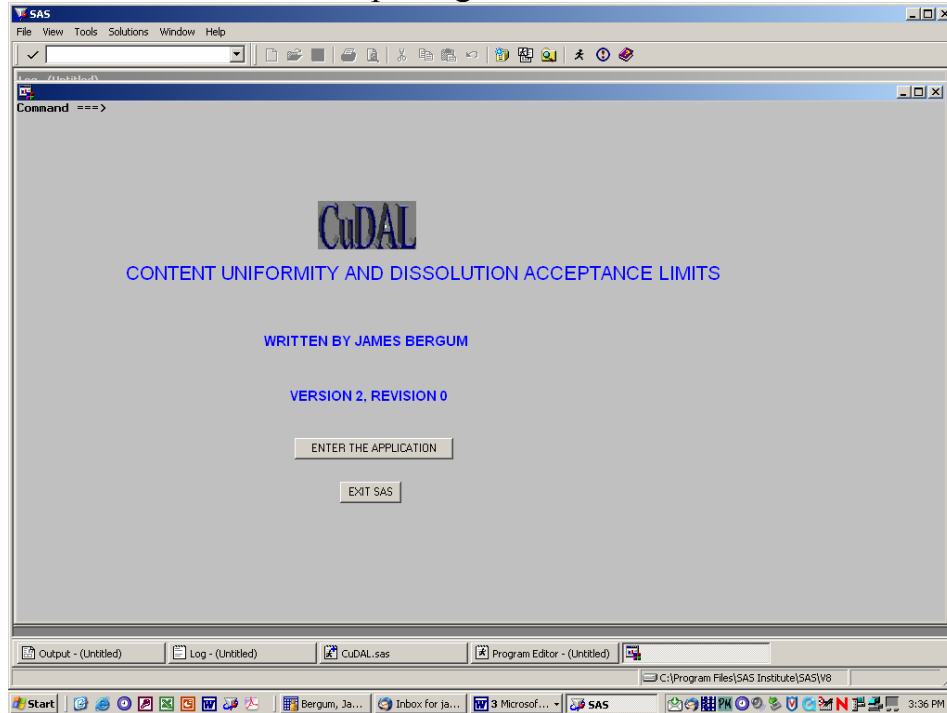
```
233.      %IF %UPCASE(&A2DISP2)=Y %THEN %DO;
234.      %EVDISP2;
235.      PROC DATASETS LIBRARY=WORK;
236.      DELETE SAVES2E;
237.      %END;
238.      %IF %UPCASE(&A3DISP2)=Y %THEN %DO;
239.      %SMPDISP2;
240.      %END;
241.      %MEND ANADISP2;

242.      %ANADISP2

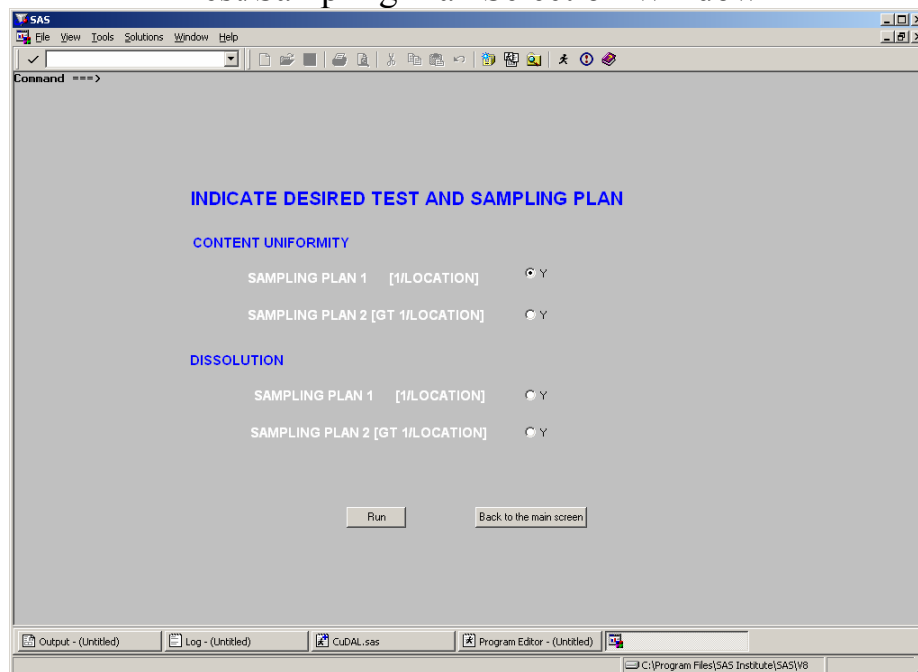
243.      RUN;
244.      %MEND DISP2;
245.      %DISP2
```

APPENDIX B WINDOWS

Opening Window:



Test/Sampling Plan Selection Window



Content Uniformity/Sampling Plan 1 Initial Window

Command ===> |

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

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

Run Cancel

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

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

Start | ... | 3:43 PM

Evaluation Sub-Window

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\VB8

Start | ... | 3:44 PM

Lower Bound for Sample Result Sub-Window

This screenshot shows the SAS 'Lower Bound for Sample Result Sub-Window'. The window 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 window contains the following text and input fields:

TO DETERMINE LOWER BOUND FOR
FOUND SAMPLE RESULTS

ENTER SAMPLE MEAN (% CLAIM):

ENTER SAMPLE CV (%):

At the bottom of the main area are two buttons: 'Run' and 'Cancel'.

The status bar at the bottom of the window shows the following tabs: 'Output - (Untitled)', 'Log - (Untitled)', 'CuDAL.sas', and 'Program Editor - (Untitled)'. The status bar also displays the file path 'C:\Program Files\SAS Institute\SAS\V8' and the time '3:45 PM'.

Content Uniformity/Sampling Plan 2 Initial Screen

This screenshot shows the SAS 'Content Uniformity/Sampling Plan 2 Initial Screen'. The window 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 window contains the following text and input fields:

CONTENT UNIFORMITY ACCEPTANCE LIMIT PROGRAM FOR
SAMPLING PLAN 2 (GREATER THEN ONE SAMPLE PER LOCATION)

ENTER NUMBER OF LOCATIONS:

ENTER NUMBER PER LOCATION:

ENTER TARGET:

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 main area are two buttons: 'Run' and 'Cancel'.

The status bar at the bottom of the window shows the following tabs: 'Output - (Untitled)', 'Log - (Untitled)', 'CuDAL.sas', and 'Program Editor - (Untitled)'. The status bar also displays the file path 'C:\Program Files\SAS Institute\SAS\V8' and the time '3:46 PM'.

Evaluation Sub-Window

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 [Taskbar icons] 3:47 PM

Lower Bound for Sample Result Sub-Window

Command ==>

TO DETERMINE LOWER BOUND FOR FOUND SAMPLE RESULTS

ENTER SAMPLE MEAN (% CLAIM): 100

ENTER SAMPLE WITHIN STD DEV (% CLAIM): 2.2

ENTER SAMPLE BETWEEN STD DEV (% CLAIM): 2.46

(I.E. STANDARD DEVIATION OF SAMPLE LOCATION MEANS)

Run Cancel

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

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

Start [Taskbar icons] 3:47 PM

Dissolution/Sampling Plan 1 Initial Window

Command ==>

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

ENTER Q VALUE: 80

ENTER SAMPLE SIZE: 6

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\V8

Start SAS 3:49 PM

Evaluation Window

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\V8

Start SAS 3:49 PM

Lower Bound for Sample Result Sub-Window

Command ==> |

TO DETERMINE LOWER BOUND FOR
FOUND SAMPLE RESULTS

ENTER SAMPLE MEAN (% CLAIM): 100

ENTER SAMPLE CV (%): 4

Run Cancel

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

C:\Program Files\SAS Institute\SAS\V8 3:49 PM

Dissolution/Sampling Plan 2 Initial Window

Command ==> |

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

ENTER O: 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\V8 3:50 PM

Evaluation Sub-Window

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\V8

Start [Taskbar Icons] 3:50 PM

Lower Bound for Sample Result Sub-Window

Command ==>

TO DETERMINE LOWER BOUND FOR FOUND SAMPLE RESULTS

ENTER SAMPLE MEAN (% CLAIM): 100

ENTER SAMPLE WITHIN STD DEV (% CLAIM): 2.2

ENTER SAMPLE BETWEEN STD DEV (% CLAIM): 2.46

(I.E. STANDARD DEVIATION OF SAMPLE LOCATION MEANS)

Run Cancel

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

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

Start [Taskbar Icons] 3:50 PM

APPENDIX C

DEFAULT WINDOW OUTPUT

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

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]

	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

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

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) J

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]

12.25

12.50

12.75

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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												
13.00												
13.25												
13.50												

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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 (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 D NAVIGATION & ERROR CHECKS

Navigation (See Appendix B for window displays and names):

Test	Window	Instruction	Expected Result	Found Result	Agree (Y or N)
1	Opening Window	'Exit SAS'	Exit's SAS		
2	Opening Window	'Enter the Application'	Opens Test/Sampling Plan Selection Window		
	Test/Sampling Plan Selection Window	Select Content Uniformity - Sampling Plan 1	Opens Initial Content Uniformity Sampling Plan 1 Window		
	Initial Content Uniformity Sampling Plan 1 Window	Select 'Cancel'	Returns to Test/Sampling Plan Selection Window		
	Test/Sampling Plan Selection Window	Select Content Uniformity - Sampling Plan 1	Opens Initial Content Uniformity Sampling Plan 1 Window		
	Initial Content Uniformity Sampling Plan 1 Window	Select Yes to Print Table, Evaluate Table, and Find Lower Bound for a sample result. Select 'Run'	Opens Evaluation Sub-Window		
	Evaluation Sub-Window	Select 'Run'	Opens Lower Bound for Sample Result Sub-Window		
	Sample Result Sub-Window	Select 'Run'	Returns to Initial Content Uniformity Sampling Plan 1 Window		
	Initial Content Uniformity Sampling Plan 1 Window	Select 'Cancel'	Returns to Test/Sampling Plan Selection Window		
	Test/Sampling Plan Selection Window	Select 'Cancel'	Returns to Opening Window		
3	Opening Window	Select 'Enter the Application', Select Content Uniformity - Sampling Plan 2	Opens Initial Content Uniformity Sampling Plan 2 Window		
	Initial Content Uniformity Sampling Plan 2 Window	Select 'Cancel'	Returns to Test/Sampling Plan Selection Window		
	Test/Sampling Plan Selection Window	Select Content Uniformity - Sampling Plan 2	Opens Initial Content Uniformity Sampling Plan 2 Window		
	Initial Content Uniformity Sampling Plan 2 Window	Select Yes to Print Table, Evaluate Table, and Find Lower Bound for a sample result. Select 'Run'	Opens Evaluation Sub-Window		
	Evaluation Sub-Window	Select 'Run'	Opens Lower Bound for Sample Result Sub-Window		
	Sample Result Sub-Window	Select 'Run'	Returns to Initial Content Uniformity		

			Sampling Plan 2 Window		
	Initial Content Uniformity Sampling Plan 2 Window	Select 'Cancel'	Returns to Test/Sampling Plan Selection Window		
	Test/Sampling Plan Selection Window	Select 'Cancel'	Returns to Opening Window		
4	Opening Window	Select 'Enter the Application', Select Dissolution - Sampling Plan 1	Opens Initial Dissolution - Sampling Plan 1 Window		
	Initial Dissolution Sampling Plan 1 Window	Select 'Cancel'	Returns to Test/Sampling Plan Selection Window		
	Test/Sampling Plan Selection Window	Select Dissolution - Sampling Plan 1	Opens Initial Dissolution Sampling Plan 1 Window		
	Initial Dissolution Sampling Plan 1 Window	Select Yes to Print Table, Evaluate Table, and Find Lower Bound for a sample result. Select 'Run'	Opens Evaluation Sub-Window		
	Evaluation Sub-Window	Select 'Run'	Opens Lower Bound for Sample Result Sub-Window		
	Sample Result Sub-Window	Select 'Run'	Returns to Initial Dissolution Sampling Plan 1 Window		
	Initial Dissolution Sampling Plan 1 Window	Select 'Cancel'	Returns to Test/Sampling Plan Selection Window		
	Test/Sampling Plan Selection Window	Select 'Cancel'	Returns to Opening Window		
5	Opening Window	Select 'Enter the Application', Select Dissolution - Sampling Plan 2	Opens Initial Dissolution Sampling Plan 2 Window		
	Initial Dissolution Sampling Plan 2 Window	Select 'Cancel'	Returns to Test/Sampling Plan Selection Window		
	Test/Sampling Plan Selection Window	Select Dissolution - Sampling Plan 2	Opens Initial Dissolution Sampling Plan 2 Window		
	Initial Dissolution Sampling Plan 2 Window	Select Yes to Print Table, Evaluate Table, and Find Lower Bound for a sample result. Select 'Run'	Opens Evaluation Sub-Window		
	Evaluation Sub-Window	Select 'Run'	Opens Lower Bound for Sample Result Sub-Window		
	Sample Result Sub-Window	Select 'Run'	Returns to Initial Dissolution Sampling Plan 2 Window		
	Initial Dissolution Sampling Plan 1 Window	Select 'Cancel'	Returns to Test/Sampling Plan Selection Window		
	Test/Sampling Plan Selection Window	Select 'Cancel'	Returns to Opening Window		

**APPENDIX D
WINDOW INPUT ERROR CHECKING
TEST DATA**

**CONTENT UNIFORMITY
SAMPLING PLAN 1**

Window	Requested Input	User Input	EXPECTED RESPONSE	FOUND RESPONSE	AGREE? (Y or N)
			N = NONE	N or ES	
			ES = ERROR SCREEN		
Initial Window	Sample Size	5	N		
		4	ES		
		2000	N		
	Bound	50	N		
		99	N		
		49.9	ES		
		99.1	ES		
		75	N		
	Confidence Interval	50	N		
		99	N		
		49.9	ES		
		99.1	ES		
		65	N		
Evaluate Sub Window	Lower Bound Mean	0	ES		
	Upper Bound Mean	0	ES		
	Increment Mean	0	ES		
	Lower Bound CV	0	ES		
	Upper Bound CV	0	ES		
	Increment CV	0	ES		
Lower Bound Based on Sample Result	Sample Mean	85.1	N		
		114.9	N		
		85	ES		
		115	ES		
		100.123	N		
	Sample CV	0.1	N		
		0	ES		
		15	N		
		-3	ES		

**CONTENT UNIFORMITY
SAMPLING PLAN 2**

Window	Requested Input	User Input	EXPECTED RESPONSE	FOUND RESPONSE	AGREE? (Y or N)
			N = NONE	N or ES	
			ES = ERROR SCREEN		
Initial Window	Number of Locations	3	N		
		2	ES		
		2000	N		
	Number per location	2	N		
		1	ES		
		2000	N		
	Bound	50	N		
		99	N		
		49.9	ES		
		99.1	ES		
		80	N		
	Confidence Level	50	N		
		99	N		
		49.9	ES		
		99.1	ES		
		70	N		
Evaluate Sub-Window	Lower Bound Mean	0	ES		
	Upper Bound Mean	0	ES		
	Increment Mean	0	ES		
	Lower Bound Within SD	0	ES		
	Upper Bound Within SD	0	ES		
	Increment Within SD	0	ES		
	Lower Bound Between SD	0	ES		
	Upper Bound Between SD	0	ES		
	Increment Between SD	0	ES		
Lower Bound Based on Sample Result	Sample Mean	85.1	N		
		114.9	N		
		85	ES		
		115	ES		
		100.123	N		
	Sample Within SD	0.1	N		
		0	ES		
		15	N		
		-3	ES		
	Sample Between SD	0.1	N		
		0	ES		
		15	N		
		-3	ES		

**DISSOLUTION
SAMPLING PLAN 1**

Window	Requested Input	User Input	EXPECTED RESPONSE	FOUND RESPONSE	AGREE? (Y or N)
			N = NONE	N or ES	
			ES = ERROR SCREEN		
Initial Window	Q	40	N		
		95	N		
		39.9	ES		
		95.1	ES		
	Sample Size	3	N		
		2	ES		
		2000	N		
	Bound	50	N		
		99	N		
		49.9	ES		
		99.1	ES		
		75	N		
	Confidence Level	50	N		
		99	N		
		49.9	ES		
		99.1	ES		
		80	N		
Evaluate Sub Window	Lower Bound Mean	0	ES		
	Upper Bound Mean	0	ES		
	Increment Mean	0	ES		
	Lower Bound CV	0	ES		
	Upper Bound CV	0	ES		
	Increment CV	0	ES		
Lower Bound Based on Sample Result	Sample Mean	75.1	N		
	(Q = 75)	100	N		
		85.5	N		
		75	ES		
	Sample CV	0.1	N		
		0	ES		
		15	N		
		-3	ES		

**DISSOLUTION
SAMPLING PLAN 2**

Window	Requested Input	User Input	EXPECTED RESPONSE	FOUND RESPONSE	AGREE? (Y or N)
			N = NONE	N or ES	
			ES = ERROR SCREEN		
Initial Window	Q	40	N		
		95	N		
		39.9	ES		
		95.1	ES		
	Number of Locations	3	N		
		2	ES		
		2000	N		
	Number per Location	2	N		
		1	ES		
		2000	N		
	Bound	50	N		
		99	N		
		49.9	ES		
		99.1	ES		
		65	N		
	Confidence Level	50	N		
		99	N		
		49.9	ES		
		99.1	ES		
		80	N		
Evaluate Sub-Window	Lower Bound Mean	0	ES		
	Upper Bound Mean	0	ES		
	Increment Mean	0	ES		
	Lower Bound Within SD	0	ES		
	Upper Bound Within SD	0	ES		
	Increment Within SD	0	ES		
	Lower Bound Between SD	0	ES		
	Upper Bound Between SD	0	ES		
	Increment Between SD	0	ES		
Lower Bound Based on Sample Result	Sample Mean	60.1	N		
	(Q = 60)	100	N		
		80.6	N		
		60	ES		
	Sample Within SD	0.1	N		
		0	ES		
		15	N		
		-3	ES		
	Sample Between SD	0.1	N		
		0	ES		
		15	N		
		-3	ES		

APPENDIX E

LOWER BOUND CALCULATIONS

The calculations used for Content Uniformity are described below:

The revised content uniformity test is a two stage test. The uniformity of dosage units for the revised test can be demonstrated by either of two methods - Content Uniformity or Weight Variation. The derivations that follow are based on the individual dosage values obtained by either of the two methods. Let S_i be the criteria of passing stage i , $i=1,2$. To meet the content uniformity test, test 10 dosage units and the requirements are met if S_1 is satisfied. Otherwise, test the next 20 units. The requirements are met if S_2 is satisfied.

Let $L_1 = 15$. The criteria of S_1 and S_2 are as follows:

S_1 = The acceptance value (defined below) of the first 10 dosage units is $\leq L_1$

- S_2 = i) The acceptance value of the 30 dosage units is $\leq L_1$
- ii) No dosage unit deviates from the calculated value of M (defined below) by more than 25% of M

T 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. We now define M as follows:

When $T \leq 101.5$

$$\begin{aligned} \text{Then } M &= \max\{98.5, \bar{X}\} \text{ if } \bar{X} \leq 100 \\ M &= \min\{101.5, \bar{X}\} \text{ if } \bar{X} > 100 \end{aligned}$$

When $T > 101.5$

$$\begin{aligned} \text{Then } M &= \max\{98.5, \bar{X}\} \text{ if } \bar{X} \leq 100 \\ M &= \min\{T, \bar{X}\} \text{ if } \bar{X} > 100 \end{aligned}$$

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

Where $k = 2.4$ for $n=10$; $k = 2.0$ for $n=30$

s is the standard deviation of the observations.

Unless otherwise specified, all the measurements of dosage units and criteria values (such as L_1 and L_2) are in percentage label claim.

Lower Probability Bound of Passing USP

Notice that

$$\begin{aligned} P(\text{passing ICH test}) &= P(S_1 \text{ or } (\bar{S}_1 \text{ and } S_2)) \\ &= P(S_1) + P(\bar{S}_1 \text{ and } S_2) - P(S_1 \text{ and } (\bar{S}_1 \text{ and } S_2)) \\ &= P(S_1) + P(\bar{S}_1 \text{ and } S_2), \end{aligned}$$

where P denotes probability and \bar{S}_1 denotes failing S_1 .

Using the fact that $P(S_1) + P(\bar{S}_1 \text{ and } S_2) \geq P(S_1)$

and $P(S_1) + P(\bar{S}_1 \text{ and } S_2) \geq P(S_1 \text{ and } S_2) + P(\bar{S}_1 \text{ and } S_2) = P(S_2)$

we have $P(\text{passing ICH test}) \geq \max\{P(S_1), P(S_2)\}$.

Denote the sample measurements of dosage units as $X_i, i=1, \dots, n$. Assume that the X_i 's follow a normal distribution with $N(\mu, \sigma)$. Then the values of $P(S_1)$ and $P(S_2)$ can be calculated as described in the following two subsections.

Computation of $P(S_1)$. Due to the definition of acceptance value, it can be seen that

For $T \leq 101.5$

$$\text{Acceptance Value} = \begin{cases} 98.5 - \bar{X} + ks & \text{if } \bar{X} < 98.5 \\ ks & \text{if } 98.5 \leq \bar{X} \leq 101.5 \\ \bar{X} - 101.5 + ks & \text{if } \bar{X} > 101.5 \end{cases}$$

For $T > 101.5$

$$\text{Acceptance Value} = \begin{cases} 98.5 - \bar{X} + ks & \text{if } \bar{X} < 98.5 \\ ks & \text{if } 98.5 \leq \bar{X} \leq T \\ \bar{X} - T + ks & \text{if } \bar{X} > T \end{cases}$$

For $T \leq 101.5$,

$$P(S_1) = P(98.5 \leq \bar{X} \leq 101.5 \text{ and } k_1 s < L_1) \\ + P(\bar{X} > 101.5 \text{ and } \bar{X} - 101.5 + k_1 s < L_1) \\ + P(\bar{X} < 98.5 \text{ and } 98.5 - \bar{X} + k_1 s < L_1),$$

where $k_1 = 2.4$.

By the central Limit Theorem, $\bar{X} = \frac{1}{n} \sum_{i=1}^n X_i$ follows a normal distribution with mean μ and standard deviation σ / \sqrt{n} denoted as $N(\mu, \sigma / \sqrt{n})$. Also $(n-1)s^2/\sigma^2$ follows a χ^2 distribution with $n-1$ degrees of freedom where

$$\text{standard deviation } s = \sqrt{\frac{1}{n-1} \sum_{i=1}^n (X_i - \bar{X})^2}$$

\bar{X} and S^2 are independent variables. The joint density of (\bar{X}, s^2) can be calculated by the product of their densities.

Denote $Z_1 = \bar{X}$ and $Z_2 = (n-1)s^2/\sigma^2$.

The density functions $f(Z_1)$ and $f(Z_2)$ are

$$f(Z_1 = z_1) = \frac{1}{\sigma \sqrt{2\pi}} e^{-\frac{(z_1 - \mu)^2}{2\sigma^2}}$$

$$f(Z_2 = z_2) = \frac{1}{\Gamma(r/2) 2^{r/2}} z_2^{r/2-1} e^{-z_2/2} \text{ for } z_2 \geq 0.$$

where $\gamma = n-1$ and $\Gamma(p) = \int_0^\infty t^{p-1} e^{-t} dt$.

The density function of Z_2 is a Chi-Square distribution with $n-1$ degrees of freedom and is denoted as $\chi^2_{(n-1)}$.

The joint density function is $f(z_1, z_2) = f(z_1) f(z_2)$,

Due to the independency of Z_1 and Z_2 , $P(S_1)$ in terms of Z_1 and Z_2 , can be rewritten as

$$P(S_1) = P(98.5 \leq Z_1 \leq 101.5 \text{ and } k_1 \sigma \sqrt{\frac{Z_2}{(n-1)}} < L_1)$$

$$\begin{aligned}
& + P(Z_1 > 101.5 \text{ and } Z_1 - 101.5 + k_1 \sigma \sqrt{\frac{Z_2}{(n-1)}} < L_1) \\
& + P(Z_1 < 98.5 \text{ and } 98.5 - Z_1 + k_1 \sigma \sqrt{\frac{Z_2}{(n-1)}} < L_1) \\
& = I_1 + I_2 + I_3,
\end{aligned}$$

where

$$\begin{aligned}
I_1 &= P(98.5 \leq Z_1 \leq 101.5 \text{ and } k_1 \sigma \sqrt{\frac{Z_2}{(n-1)}} < L_1) \\
I_2 &= P(Z_1 > 101.5 \text{ and } Z_1 - 101.5 + k_1 \sigma \sqrt{\frac{Z_2}{(n-1)}} < L_1) \\
I_3 &= P(Z_1 < 98.5 \text{ and } 98.5 - Z_1 + k_1 \sigma \sqrt{\frac{Z_2}{(n-1)}} < L_1)
\end{aligned}$$

Notice that

$$\begin{aligned}
I_1 &= P(98.5 \leq Z_1 \leq 101.5) * P(k_1 \sigma \sqrt{\frac{Z_2}{(n-1)}} < L_1) \\
&= (\Phi(t_1) - \Phi(t_2)) * P(Z_2 < (n-1) * L_1^2 / (k_1^2 \sigma^2))
\end{aligned}$$

with $t_1 = \sqrt{n}(101.5 - \mu) / \sigma$ and $t_2 = \sqrt{n}(98.5 - \mu) / \sigma$

and Φ the cumulative density function of standard normal $N(0,1)$.

Let $g(z_1) = (n-1) * (L_1 + 101.5 - z_1)^2 / (k_1 \sigma)^2$. Noting that that $L_1 = 15$, we have

$$\begin{aligned}
I_2 &= P(Z_1 > 101.5 \text{ and } Z_2 < g(Z_1)) \\
&= \int_{101.5}^{101.5+15} f(z_1) \int_0^{g(z_1)} f(z_2) dz_2 dz_1
\end{aligned} \tag{1}$$

Let $h(z_1) = (n-1)(L_1 - 98.5 + z_1)^2 / (k_1 \sigma)^2$. Then

$$I_3 = P(Z_1 < 98.5 \text{ and } Z_2 < h(Z_1))$$

$$= \int_{98.5-15}^{98.5} f(z_1) \int_0^{h(z_1)} f(z_2) dz_2 dz_1 \quad (2)$$

The integrations of (1) and (2) have no analytical results due to the complexities of their integrands. However, numerical results of the integrations can be calculated. For a Chi-Square distribution with k degrees of freedom, the function PROBCHI(y,k) in SAS provides the numerical result of integration $\int_0^y f(z_2) dz_2$ for given y. Taking advantage of known function PROBCHI(y,k), the numerical integrations of (1) and (2) are calculated as follows:

$$I_2 = \lim_{h \rightarrow 0} \sum_{i=1}^K (\Phi(Z_1 + ih) - \Phi(Z_1 + (i-1)h)) \text{PROBCHI}(g(Z_1 + (i-1/2)h), n-1)$$

where $K = \lceil L_1/h \rceil$, the number of intervals of width h. Similarly, for I_3 ,

$$I_3 = \lim_{h \rightarrow 0} \sum_{i=1}^K (\Phi(Z_1 + ih) - \Phi(Z_1 + (i-1)h)) \text{PROBCHI}(h(Z_1 + (i-1/2)h), n-1)$$

A small program in SAS can be programmed to carry out the calculation. Therefore, $P(S_1)$ can be calculated as

$$P(S_1) = (\Phi(t_1) - \Phi(t_2)) * P(Z_2 < (n-1) * L_1^2 / (k_1^2 \sigma^2)) + I_2 + I_3$$

A similar calculation can be performed for $T > 101.5$ by replacing 101.5 in the above equations with T.

Computation of $P(S_2)$ There are two sub-criteria in S_2 which are denoted as C_{21} and C_{22} respectively as follows:

C_{21} = AV of the 30 dosage units is less than or equal to L_1 .

C_{22} = No unit deviates from the calculated value of M by more than 25% of M.

Using the inequality that, for two events A and B,

$$P(A \text{ and } B) = P(A) + P(B) - P(A \text{ or } B) \geq P(A) + P(B) - 1.$$

One gets $P(S_2) = P(C_{21} \text{ and } C_{22}) \geq \max\{P(C_{21}) + P(C_{22}) - 1, 0\}$

Since criteria C_{21} is very similar to S_1 except for $n=30$ and $k=2.0$ in the former while $n=10$ and $k=2.4$ in the later, the calculation of $P(C_{21})$ is carried out similarly as in $P(S_1)$ with $n=30$ and $k=2.0$. Therefore,

$$P(C_{21}) = (\Phi(t_1) - \Phi(t_2)) * P(Z_2 < (n-1) * L_1^2 / (k_2^2 \sigma^2))$$

$$\begin{aligned}
& + \lim_{h \rightarrow 0} \sum_{i=1}^K (f(z_1 + ih) - f(z_1 + (i-1)h)) \text{PROBCHI}(g(z_1 + (i-1/2)h), n-1) \\
& + \lim_{h \rightarrow 0} \sum_{i=1}^K (f(z_1 + ih) - f(z_1 + (i-1)h)) \text{PROBCHI}(h(z_1 + (i-1/2)h), n-1)
\end{aligned}$$

where $n = 30$ and $k_2 = 2.0$. For the calculation of $P(C_{22})$, notice that

For $T \leq 101.5$

$$M = \begin{cases} 98.5 & \text{if } \bar{X} < 98.5 \\ \bar{X} & \text{if } 98.5 \leq \bar{X} \leq 101.5 \\ 101.5 & \text{if } \bar{X} > 101.5 \end{cases}$$

Then

$$\begin{aligned}
P(C_{22}) & \geq P(98.5 \leq \bar{X} \leq 101.5 \text{ and } |X_i - \bar{X}| < 0.25*98.5, i = 1, \dots, n) \\
& + P(\bar{X} > 101.5 \text{ and } |X_i - 101.5| < 0.25*101.5, i = 1, \dots, n) \\
& + P(\bar{X} < 98.5 \text{ and } |X_i - 98.5| < 0.25*98.5, i = 1, \dots, n) \\
& = P(98.5 \leq \bar{X} \leq 101.5 \text{ and } \bar{X} - 24.625 < X_i < \bar{X} + 24.625, i = 1, \dots, n) \\
& + P(\bar{X} > 101.5 \text{ and } 101.5 - 25.375 < X_i < 101.5 + 25.375, i = 1, \dots, n) \\
& + P(\bar{X} < 98.5 \text{ and } 98.5 - 24.625 < X_i < 98.5 + 24.625, i = 1, \dots, n) \\
& \geq P(101.5 - 24.625 < X_i < 98.5 + 24.625, i = 1, \dots, n) \\
& = [\Phi((98.5 + 24.625 - \mu)/\sigma) - \Phi((101.5 - 24.625 - \mu)/\sigma)]^n
\end{aligned}$$

For $T > 101.5$

$$M = \begin{cases} 98.5 & \text{if } \bar{X} < 98.5 \\ \bar{X} & \text{if } 98.5 \leq \bar{X} \leq T \\ T & \text{if } \bar{X} > T \end{cases}$$

Then

$$\begin{aligned} P(C_{22}) &\geq \begin{aligned} &P(98.5 \leq \bar{X} \leq T \quad \text{and } |X_i - \bar{X}| < 0.25*98.5, i = 1, \dots, n) \\ &+ P(\bar{X} > T \quad \text{and } |X_i - T| < 0.25*T, i = 1, \dots, n) \\ &+ P(\bar{X} < 98.5 \quad \text{and } |X_i - 98.5| < 0.25*98.5, i = 1, \dots, n) \end{aligned} \\ &= \begin{aligned} &P(98.5 \leq \bar{X} \leq T \quad \text{and } \bar{X} - 24.625 < X_i < \bar{X} + 24.625, i = 1, \dots, n) \\ &+ P(\bar{X} > T \quad \text{and } T - 0.25*T < X_i < T + 0.25*T, i = 1, \dots, n) \\ &+ P(\bar{X} < 98.5 \quad \text{and } 98.5 - 24.625 < X_i < 98.5 + 24.625, i = 1, \dots, n) \end{aligned} \\ &\geq P(T - 24.625 < X_i < 98.5 + 24.625, i = 1, \dots, n) \\ &= [\Phi((98.5 + 24.625 - \mu)/\sigma) - \Phi((T - 24.625 - \mu)/\sigma)]^n \end{aligned}$$

A lower bound of the probability of passing ICH requirements is $P(\text{Passing ICH}) \geq \max\{P(S_1), P(S_2)\}$

The USP dissolution test and calculations are as follows:

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

Pass if the following criteria are met:

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

Calculation:

$P(\text{meeting criteria of stage 1})$

$$= [P(x \geq Q + 5)]^6$$

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 $\leq Q - 15$

Calculation:

P(passing 1st criteria of stage 2)

$$= P(\text{Mean} \geq Q)$$

P(passing 2nd criteria of stage 2)

$$= [P(x \geq Q - 15)]^{12}$$

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 $\leq Q - 25$

Calculation:

P(passing 1st criteria of stage 3)

$$= P(\text{Mean result} \geq Q)$$

P(passing 2nd criteria of stage 3)

$$= [P(x \geq Q - 15)]^{24} \\ + 24 [P(Q - 25 \leq x \leq Q - 15)] [P(x \geq Q - 15)]^{23} \\ + 276 [P(Q - 25 \leq x \leq Q - 15)]^2 [P(x \geq Q - 15)]^{22}$$

APPENDIX F

PROGRAM DESCRIPTION

Each of the five programs (excludes programs for GUI) included in CuDAL are described below. Macros are italicized. To aid in locating the macro's and windows in the SASTM programs, brackets enclose the associated program line numbers.

PROGRAM: CuDAL.SAS - Used to define file locations

The file CuDAL.SAS shown below provides the location of the four analysis macro's (CUSP1.SAS, CUSP2.SAS, DISP1.SAS, and DISP2.SAS) and the two files for the GUI interface/navigation (cudal.sas7bcat and Files.sas.org). In each of these lines of code, the user replaces D:\V2 with the appropriate directory locations. This is the only file that requires editing.

```
1. ***** LIBRARY FOR THE APPLICATION*****;
2. /* deleting the macro variables */
3. data vars;
      i. set sashelp.vmacro;
4. run;
5. data _null_;
      i. set vars;
      ii. if scope='GLOBAL' and name ^= 'SYSODSPATH' then
      iii. call execute('%symdel '||trim(left(name))||' ');
6. run;

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

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

PROGRAM: CUSP1.SAS - Used to generate Content Uniformity acceptance limits using Sampling Plan 1

The macros contained in CUSP1.SAS are described below:

c1calc [52-162]-

This macro is used to calculate the lower bound on passing the USP content uniformity test given a pair of specific values for μ and σ . The macro *calculuspl* passes two points in the confidence region for μ and σ to evaluate. Both of these points have the largest value of σ (SIGMA) in the confidence region. One point has the smallest value of μ (LLU) and the other the largest value for μ (ULU). The pair LLU, SIGMA is evaluated first, then the pair ULU, SIGMA. PROB NORM is used to calculate the probability of meeting the CV criteria and

to calculate the normal probability of an individual value falling within a given interval. Since the probability of passing the USP test is greater than or equal to the probability of passing any individual stage, the maximum probability of passing is selected from stage 1 (LPROB1) and stage 2 (LPROB2) for each point. Finally, the lowest probability of passing the USP test occurs with the pair with the lowest probability of passing so the minimum probability (OVERBD) is selected from the two evaluated points.

*calcu*sp1[163-228]-

This macro determines the largest value for the sample CV such that for all points in the confidence region for μ and σ , the probability of passing the USP test for content uniformity is greater than the user specified lower bound (LBOUND). The confidence interval is a triangle. The only two points to evaluate on the triangle are the two points with the maximum value of sigma. So, for a given value of the sample mean, the strategy is to start with a very small value for the sample standard deviation and then construct the corresponding confidence region for μ and σ . Then evaluate the two points corresponding to the largest value of σ and the smallest and largest values for μ . If both of the points result in probabilities greater than LBOUND, this means that all of the points in the entire confidence region would give a probability of passing the USP content uniformity test greater than LBOUND. Therefore, given the same sample mean, a larger value of the standard deviation can be evaluated. The value of the sample standard deviation is increased until one of the two points evaluated in the confidence region is less than LBOUND. The last value of the standard deviation is kept for the acceptance limit table. At a value of the sample mean around 100, the sample standard deviation will reach its maximum acceptance limit table value. The next sample mean evaluated after this maximum has been reached will have a lower value of the sample standard deviation. The program checks to determine when this occurs. At this point, the program starts generating the rest of the acceptance limit table by setting the sample mean to 114.9, resetting the sample standard deviation to a small value and works its way down from 114.9 to the value of the sample mean with the largest sample standard deviation.

The strategy described above is performed by using a DO loop that starts with a sample mean of 85.1 and increases to 114.9 in increments of 0.1 (set by macro variable D). The standard deviation starts at 0.01 (STARTSD) and increments by 0.001. For each value of the standard deviation (SAMPD), the upper bound for sigma (SIGMA) is calculated using the usual χ^2 based confidence bound formula. The two points in the confidence interval that will be evaluated are determined (LLU and ULU). LLU and ULU are the lower and upper ends of the confidence region associated with SIGMA. Since the sample mean and sample variance are independent, the overall α level (1- confidence level) is the product of the two individual α levels for μ and σ . So the two individual confidence levels are the square root of the overall α . Then the portion of the overall α used to estimate μ is

divided equally to construct a 2-tailed test. Since the confidence interval for σ is one-sided, the portion of the overall α for σ is all put into one tail. The macro *c1calc* is called to calculate the lower bound on the probability of passing the USP test for LLU and ULU. The minimum of the two probabilities (OVERBD) is returned from *c1calc*. If the minimum is greater than the lower bound selected by the user (LBOUND), the standard deviation (SAMPSTD) is incremented by 0.001 and a new LLU and ULU are computed and the minimum probability is found again. Once the minimum is less than the lower bound, 0.001 is subtracted from the standard deviation, and the CV is computed. A special case is when the starting value (STARTSD) of 0.01 gives a minimum less than the lower bound. In this case the CV is set to 0. The value of the standard deviation is used as a starting point for the next sample mean since the standard deviation must increase as the sample mean increases from 85.1 to around 100. At some value of the sample mean greater than 100, the standard deviation will start decreasing. In the macro, when a new sample mean is evaluated with the starting value of the previous standard deviation and the resulting OVERBD is less than the user pre-specified lower bound (LBOUND), this means that the maximum tabled sample standard deviation has been reached. Therefore, the macro saves the value of this mean (STARTM), goes to the label UPPER, sets the starting standard deviation back to 0.01, and starts a DO loop that starts with a sample mean (MEAN) at 114.9 and decreases by 0.1 to STARTM. The same procedure is used as described above to find the sample standard deviation for each sample mean.

Once the entire set of sample mean, CV combinations are determined, the data is sorted by MEAN and a data set is prepared for use in printing the table. This is done by creating six data sets. Each of these data sets contains the data for two columns of the printed acceptance table (one for the sample mean and one for the CV). Data set ONE contains the mean and CV for values of the sample mean between 85.1 and 90.0, data set TWO from 90.1 to 95.0, etc. All six of these data sets are then merged together to form data set SEVEN.

PRTCUSPI [229-241]-

This macro prints the acceptance limit table by printing out data set SEVEN prepared by the macro *calcuspl*.

EVCUSPI[242-272]-

This macro starts by defining a window (SMAIN [258-271]) for the user to specify the range of possible population values for the mean and CV. For the population mean, the user specifies the lower bound for the mean (ULOW), the upper bound for the mean (UHIGH), the increment (UINCRE), and the divisor (UDIV). Each of these values must be a positive integer. So if the user wants to evaluate population means from 98.0 to 102.0 by 0.5, the following values would be specified: ULOW = 980, UHIGH = 1020, UINCRE = 5, and UDIV = 10. The upper and lower values for the CV as well as the increment and divisor are input

in the same manner as those are for the mean. Finally, data set SEVEN is read into data set TAB. The macro DSCUSP1 [321-329] reads TAB and creates 6 data sets containing the sample means and standard deviations from TAB. The 6 data sets are appended to one another and stored in data set ONE.

The macro *SIGCUSP1* [337-362] performs the calculations for each population mean and CV combination. The strategy is as follows: The acceptance limit table consists of pairs of sample means with an upper bound on the sample CV. Data set ONE contains the sample mean and sample standard deviation pairs that make up the entire acceptance limit table. The table begins with a sample mean of 85.1 and ends with a sample mean of 114.9. To calculate the probability of passing the acceptance limit table for specified values for the population mean and population CV, the probability is calculated of a sample mean falling between adjacent means in the table and the sample standard deviation falling below the average standard deviation at the two endpoints. So, suppose the standard deviation at a sample mean of 85.1 was 0.2 and the sample standard deviation bound at a sample mean of 85.2 was 0.5. If the evaluation was at a population mean of 100 with standard deviation of 3, then the first calculation would be to find the probability of getting a sample mean between 85.1 and 85.2 and a sample standard deviation less than $(0.2 + 0.5)/2$ or 0.35. This is done using the SAS functions - PROBNORM and PROBCHI. The second calculation would calculate the probability of getting a sample means between 85.2 to 85.3 with a sample standard deviation less than the average of the corresponding standard deviations for 85.2 and 85.3. These probabilities are summed across all the intervals from 85.1 to 114.9. The sum of these probabilities (PTRAP) is the probability of passing the table for specific population values for the mean and standard deviation. To perform the calculation, the lag function in SAS is used to obtain the previous value for the sample mean and sample standard deviation. The last value of PTRAP is output. PROC APPEND is used to save the PTRAP value for each combination of CV and U in the DO loop. These values are stored in the data set SAVEALL. Finally, the data set SAVEALL is printed.

SMPCUSP1 [273-298]

This macro is used to calculate the lower bound of passing the USP content uniformity test given the sample mean and sample standard deviation. The data set TAB determines the endpoints of the confidence interval based on the user input values for the sample mean and standard deviation and prior information such as dosage form type, confidence level, and sample size. The overall α is divided into two portions as described above in the macro *calcusp1*. The macro *clcalc* is called to determine the lower bound. Finally, the lower bound is printed.

ANACUSP1 [299-315]

This macro is used to respond to the user input from the initial test/sampling plan window. If the user requests printing of the acceptance limit table or evaluation

of a table, then the macro *calcuspl* is called. If the user requests a printout of the acceptance limit table, the macro *PRTCUSPI* is called. If an evaluation is requested, the macro *EVCUSPI* is called. After the evaluation macro is finished the dataset SAVEALL is deleted. Finally, if the user requests a lower bound for a sample mean and standard deviation, the macro *SMPCUSPI* is called.

PROGRAM: CUSP2.SAS - Content Uniformity using Sampling Plan 2

The macros contained in CUSP2.SAS are defined below:

Cullu [62-119]

This macro performs the lower probability bound calculation for the point in the confidence region with the smallest value of μ (LLU) and largest value of σ (SIGMA). The calculation is performed as in *clcalc* using the SAS function PROBNORM. Since the probability of passing the USP test is greater than or equal to the probability of passing any individual stage, the maximum probability of passing is selected from stage 1 (LPROB1) and stage 2 (TPROBL2).

Cuulu [120-177]

This macro performs the lower probability bound calculation for the point in the confidence region with the largest value of μ (ULU) and largest value of σ (SIGMA). The calculation is performed as in *clcalc* using the SAS function PROBNORM. Since the probability of passing the USP test is greater than or equal to the probability of passing any individual stage, the maximum probability of passing is selected from stage 1 (LPROB1) and stage 2 (TPROBL2).

calcusp2 [178-258]

This macro finds the acceptance limit on the CV for a given mean. The confidence interval is a triangle. The only two points to evaluate on the triangle are the two points with the maximum value of sigma. However, the value of sigma is a function of both the between and within variance components. A method to construct a confidence interval for the sum of the within and between variance components is given in Graybill, F.A. & Wang, C., "Confidence Intervals on Nonnegative Linear Combinations of Variances", Journal of the American Statistical Association, December 1980, Volume 75, Number 372, p. 869 - 873.

Let

MS_L = Mean Square Between Locations from One-Way ANOVA

MS_E = Mean Square Within Locations from One-Way ANOVA

L = Number of Locations

n = Number observations at each location

Then the upper confidence limit for the sum of the between location and within location variance components (i.e. σ) is

$$\left[\frac{1}{n} MS_L + (1 - \frac{1}{n}) MS_E \right] + \left\{ \left[\frac{1}{n} ((L - 1) / \chi^2_{L-1} - 1) MS_L \right]^2 + \left[((1 - \frac{1}{n}) L (n - 1) / \chi^2_{L(n-1)} - 1) MS_E \right]^2 \right\}^{1/2}$$

The strategy is as follows: Given the sample within location standard deviation (SE) and the sample between location standard deviation (SM), a confidence interval for σ (SIGMA) was computed using the Graybill Wang method. Since the sample mean and mean squares for the between location and within location are independent, the overall α level (1- confidence level) is the product of the two individual α levels for μ and σ . So the two individual confidence levels are the square root of the overall α . Then the portion of the overall α used to estimate μ is divided equally to construct a 2-tailed test. Since the confidence interval for σ is one-sided, the portion of the overall α for σ is all put into one tail. [Note that SM is not the between location variance component. It's the standard deviation of the location means.] Then, for increasing values of the sample mean starting at 84.9, the lower bound is calculated by calling the macro *cullu*. Once the lower bound (OVERBDL) is greater than the specified lower bound (LBOUND), the lower limit for the sample mean has been identified (MEANL) and program goes to the label UPPER to find the upper limit for the sample mean. This time the sample mean starts at 115.1, calls the macro *cuulu*, and decreases until the overall bound (OVERBU) is greater than LBOUND. The upper bound for the mean (MEANU) has been identified. So for the given values for SE and SM, the lower and upper limits for the sample mean have been found.

The SAS code is written to handle two special situations. The first is when the value of SM equals D (D is the starting value for both SM and SE in the DO loops). If SM equals D, this means that for the first value of SM, the upper bound was greater than the specified lower bound. Therefore, there is no sample mean that results in an evaluated lower bound less than the specified bound. The symbol '!' is output indicating that there is no sample mean that meets the requirements for the lower bound and confidence level specified. The second situation is if SE equals D. This means that the largest value of SM that needs to be evaluated anywhere in the table has been found. So, the code resets the largest value of SM that needs to be evaluated.

The set of means and standard deviations is stored in the data set TABC.

PRTCUSP2 [259-442]

This macro prints the acceptance limit table by reading the data set TABC, transposing it, and printing out data.

EVCUSP2 [443-479]

The between location standard deviation is the between location variance component and not the standard deviation of the location means. For the population mean, the user specifies the lower bound for the mean (ULOW), the upper bound for the mean (UHIGH), the increment (UINCRE), and the divisor (UDIV). Each of these values must be a positive integer. So if the user wants to evaluate population means from 98.0 to 102.0 by 0.5, the following values would be specified: ULOW = 980, UHIGH = 1020, UINCRE = 5, and UDIV = 10. The upper and lower values for the within location standard deviation and between location standard deviation as well as the increment and divisor are input in the same manner as those for the mean.

The macro *SIGCUSP2* performs the calculations for each population mean (U), within location standard deviation (SIGSE), between location standard deviation (SIGSM) combination. The strategy is as follows: The acceptance limit table consists of a pair of sample means for each combination of within location standard deviation (SE) and standard deviation of location means (SM). Data set TABC contains the lower limit for the sample mean (MEANL), the upper limit for the sample mean (MEANU), the value of the within location standard deviation (SE), and the standard deviation of the between location means (SM). To calculate the probability of passing the acceptance limit tables for specified values for the population mean, within location standard deviation, and between location standard deviation, the probability is calculated of a sample mean falling between the upper and lower mean limits. So, suppose one line from TABC is $se = 0.4$, $sm = 0.2$, $meanl = 98.0$, and $meanu = 101.5$. Then the program would calculate the probability that the sample mean would lie within 98.0 and 101.5, se would lie between 0.3 and 0.4, and sm would lie between 0.1 and 0.2. This is done using the SAS functions - PROBNORM and PROBCHI. The same calculation would be performed for each observation in the data set TABC. These probabilities are summed for all observation in the data set. The sum of these probabilities (PSUM) is the probability of passing the table for specific population values for the mean, within and between location standard deviations. The last value of PSUM is output. PROC APPEND is used to save the PSUM value for each combination of U, SIGSE, and SIGSM in the DO loop. These values are stored in the data set SAVES2E. Finally, the data set SAVES2E is printed.

SMPCUSP2 [480-517]

This macro is used to calculate the lower bound of passing the USP content uniformity test given the sample mean, sample within location standard deviation, and the standard deviation of location means. The data set TAB determines the endpoints of the confidence interval based on the user input values for the sample mean, sample within location standard deviation, and standard deviation of location means and prior information such as dosage form type, confidence level,

number of locations and number of samples at each location. The overall α is divided into two portions as described in the macro *calcusp2*. The macro's *cullu* and *cuulu* are called to determine the lower bound. Finally, the lower bound is printed.

ANACUSP2 [518-534]

This macro is used to respond to the user input from the chosen initial test/sampling plan window. If the user requests printing of the acceptance limit table or evaluation of a table, then the macro *calcusp2* is called. If the user requests a printout of the acceptance limit table, the macro *PRTCUSP2* is called. If an evaluation is requested, the macro *EVCUSP2* is called. After the evaluation macro is finished the dataset SAVES2E is deleted. Finally, if the user requests a lower bound for a sample mean and standard deviation, the macro *SMPCUSP2* is called.

PROGRAM: DISP1.SAS - Used to generate Dissolution acceptance limits using Sampling Plan 1

The macros contained in DISP1.SAS are defined below:

COMPUTE [51-63]

For specific values of the population mean and standard deviation, this macro performs the lower probability bound calculation.

Each time this macro is called there is one value for μ (LLU) and one value for σ (SIGMA). The pair LLU, SIGMA is evaluated. PROBNORM is used to calculate the normal probability of an individual value falling within a given interval. Since the probability of passing the USP test is greater than or equal to the probability of passing any individual stage, the maximum probability of passing is selected from stage 1 (F1), stage 2 (F2), and stage 3 (F3).

caldisp1 [64-108]

This macro finds the acceptance limit on the CV for a given sample mean. The confidence interval is a triangle. For dissolution, only one point needs to be evaluated. This is the point with the smallest value of the population mean and the maximum value of sigma. So, for a given value of the sample mean, one can just keep increasing the sample value of the standard deviation until the evaluation of the point on the triangle has a lower bound probability less than pre-specified lower bound. Also note that the probability of passing the dissolution test only depends on the distance from Q and not the actual value of Q. So, the lower bound on passing the dissolution test with a Q of 80 and sample mean of 85 would be the same as passing the dissolution test with a Q of 85 and a sample mean of 90 since they both are 5 units away from Q. Therefore, this macro generates the acceptance limits on the interval from 0 to (100 - Q). Once the table has been generated, the value of Q is added to each value of the sample mean. The table is generated by using a DO loop that starts with a sample mean of 0.2 and goes to (100 - Q) in increments of 0.2 (set by macro variable D). The standard deviation starts at 0.002 (STARTSD) and increments by 0.001. For each value of the standard deviation (SAMPSTD), the upper bound for sigma (SIGMA) is calculated using the usual confidence bound formula. The point in the confidence interval that will be evaluated is determined (LLU). LLU is the lower end of the confidence region associated with SIGMA. Since the sample mean and sample variance are independent, the overall α level (1- confidence level) is the product of the two individual α levels for μ and σ . So each of the two individual confidence levels are the square root of the overall α . The macro *COMPUTE* is called to find the lower bound on the probability of passing the USP test for LLU. If the minimum is greater than the lower bound selected by the user (LBOUND), the standard deviation (SAMPSTD) is incremented by 0.001 and a new LLU is computed and the minimum probability is found again. Once the minimum is less

than the lower bound, 0.001 is subtracted from the standard deviation, and the CV is computed. A special case is when the starting value (STARTSD) of 0.002 gives a minimum less than the lower bound. In this case the CV is set to 0. The value of the standard deviation is used as a starting point for the next sample mean since we know that the standard deviation must increase as the sample mean increases.

Once the entire set of sample mean, CV combinations are determined, the data is sorted by MEAN and a data set is prepared for use in printing the table. This is done by creating five data sets. Each of these data sets contains the data for two columns of the printed acceptance table. Data set ONE contains the mean and CV for the first fifth of the values of the sample mean, data set TWO the second fifth, etc. All five of these data sets are then merged together to form data set D1ALL.

PRTDISP1 [109-123]

This macro prints the acceptance limit table by printing out data set D1ALL prepared by the macro *caldisp1*.

EVDISP1 [124-146]

For the population mean, the user specifies the lower bound for the mean (ULOW), the upper bound for the mean (UHIGH), the increment (UINCRE), and the divisor (UDIV). Each of these values must be a positive integer. So if the user wants to evaluate population means from 90.0 to 92.0 by 0.5, the following values would be specified: ULOW = 900, UHIGH = 920, UINCRE = 5, and UDIV = 10. The upper and lower values for the CV as well as the increment and divisor are input in the same manner as those are for the mean. Finally, data set D1ALL is read into data set DI1SET. The macro DSCUSP1 reads DI1SET and creates five data sets containing the sample means and standard deviations from DI1SET. The five data sets are appended to one another and stored in data set DIONE.

The macro *SIGDISP1* performs the calculations for each population mean and CV combination. The strategy is as follows: The acceptance limit table consists of pairs of sample means with an upper bound on the sample CV. Data set DIONE contains the sample mean and sample standard deviation pairs that make up the entire acceptance limit table beginning with a sample mean of $Q + 0.2$ and ending with a sample mean of 100.0. To calculate the probability of passing the acceptance limit table for specified values for the population mean and population CV, the probability is calculated of a sample mean falling between adjacent means in the table and the sample standard deviation falling below the average standard deviation at the two endpoints. The product of these two probabilities is computed since the sample mean and sample variance are independent of one another. So, suppose the standard deviation at a sample mean of 75.2 was 0.2 and the sample standard deviation bound at a sample mean of 75.4 was 0.5. If the evaluation was at a population mean of 100 with standard deviation of 3, then the

first calculation would be to find the probability of getting a sample mean between 75.2 and 75.4 and a sample standard deviation less than $(0.2 + 0.5)/2$ or 0.35. This is done using the SAS functions - PROBNORM and PROBCHI. The second calculation would calculate the probability of getting a sample means between 75.4 to 75.6 with a sample standard deviation less than the average of the corresponding standard deviations for 75.4 and 75.6. These probabilities are summed across all the intervals from $Q + 0.2$ to 100.0. The sum of these probabilities (PTRAP) is the probability of passing the table for specific population values for the mean and standard deviation. To perform the calculation, the lag function in SAS is used to obtain the previous value for the sample mean and sample standard deviation. The last value of PTRAP is output. PROC APPEND is used to save the PTRAP value for each combination of CV and U in the DO loop. These values are stored in the data set D1SAVALL. Finally, the data set D1SAVALL is printed.

SMPDISP1 [147-172]

This macro is used to calculate the lower bound of passing the USP dissolution test given the sample mean and sample standard deviation. The data set DI1SMP determines the endpoints of the confidence interval based on the user input values for the sample mean and standard deviation and prior information such as confidence level and sample size. The macro *COMPUTE* is called to determine the lower bound. Finally, the lower bound is printed.

ANADISP1 [173-188]

This macro is used to respond to the user input from the initial window chosen from the test/sampling plan window. If the user requests printing of the acceptance limit table or evaluation of a table, then the macro *caldisp1* is called. If the user requests a printout of the acceptance limit table, the macro *PRTDISP1* is called. If an evaluation is requested, the macro *EVDISP1* is called. After the evaluation macro is finished the dataset D1SAVALL is deleted. Finally, if the user requests a lower bound for a sample mean and standard deviation, the macro *SMPDISP1* is called.

PROGRAM: DISP2.SAS - Used to generate Dissolution acceptance limits using Sampling Plan 2

The macros contained in DISP2.SAS are defined below:

COMPUTE [121-133]

For specific values of the population mean and standard deviation, this macro performs the lower probability bound calculation.

Each time this macro is called there is one value for μ (LLU) and one value for σ (SIGMA). The pair LLU, SIGMA is evaluated. PROBNORM is used to calculate the normal probability of an individual value falling within a given interval. Since the probability of passing the USP test is greater than or equal to the probability of passing any individual stage, the maximum probability of passing is selected from stage 1 (F1), stage 2 (F2), and stage 3 (F3).

caldisp2 [137-198]

This macro finds the acceptance limit on the CV for a given mean. The confidence interval is a triangle. The only point to evaluate on the triangle is the point with the smallest value of the population mean and the maximum value of sigma. However, the value of sigma is a function of both the between and within variance components. The confidence interval for the sum of the within and between variance components uses the Graybill, F.A. & Wang, C. method described above in the macro *calcusp2* of the content uniformity section for sampling plan 2. Since the sample mean and mean squares for the between location and within location are independent, the overall α level (1- confidence level) is the product of the two individual α levels for μ and σ . So the two individual confidence levels are the square root of the overall α .

The strategy was as follows: Given the sample within location standard deviation (SE) and the sample between location standard deviation (SM), a confidence interval for σ (SIGMA) was computed using the Graybill Wang method. Then, for increasing values of the sample mean starting at 0.2, the lower bound was calculated by calling the macro *COMPUTE*. Once the lower bound (OVERBD) is greater than the specified lower bound (LBOUND), the lower limit for the sample mean has been found (MEANL) for the given values of SE and SM.

As described in *calcusp2*, the SAS code is written to handle two special situations when either the value of SM or SE equals D.

These values are stored in the data set TABD.

PRTDISP2 [200-218]

This macro prints the acceptance limit table using the SAS procedure PROC TABULATE by reading the data set TABD and printing the output.

EVDISP2 [221-362]

For the population mean, the user specifies the lower bound for the mean (ULOW), the upper bound for the mean (UHIGH), the increment (UINCRE), and the divisor (UDIV). Each of these values must be a positive integer. So if the user wants to evaluate population means from 90.0 to 92.0 by 0.5, the following values would be specified: ULOW = 900, UHIGH = 920, UINCRE = 5, and UDIV = 10. The upper and lower values for the within location standard deviation and between location standard deviation as well as the increment and divisor are input in the same manner as those for the mean.

The macro *SIGDISP2* [312-346] performs the calculations for each population mean (U), within location (SIGSE), between location (SIGSM) combination. The strategy is as follows: The acceptance limit table consists of a sample mean for each combination of within location standard deviation (SE) and standard deviation of location means (SM). Data set TABD contains the lower limit for the sample mean (MEANL), the value of the within location standard deviation (SE), and the standard deviation of the between location means (SM). To calculate the probability of passing the acceptance limit tables for specified values for the population mean, within location standard deviation, and between location standard deviation, the probability is calculated of a sample mean falling above lower mean limit. So, suppose one line from TABD is se = 0.4, sm = 0.2 and meanl = 98.0. Then the program would calculate the probability that the sample mean would be greater than 98.0, se would lie between 0.3 and 0.4, and sm would lie between 0.1 and 0.2. This is done using the SAS functions - PROBNORM and PROBCHI. The same calculation would be performed for each observation in the data set TABD. These probabilities are summed for all observation in the data set. The sum of these probabilities (PSUM) is the probability of passing the table for specific population values for the mean, within and between location standard deviations. The last value of PSUM is output. PROC APPEND is used to save the PSUM value for each combination of U, SIGSE, and SIGSM in the DO loop. These values are stored in the data set SAVES2E. Finally, the data set SAVES2E is printed.

SMPDISP2 [364-440]

This macro is used to calculate the lower bound of passing the USP dissolution test given the sample mean, sample within location standard deviation, and the standard deviation of location means. The data set TAB determines the endpoints

of the confidence interval based on the user input values for the sample mean, sample within location standard deviation, and standard deviation of location means and prior information such as confidence level, number of locations and number of samples at each location. The macro COMPUTE is called to determine the lower bound. Finally, the lower bound is printed.

ANADISP2 [442-456]

This macro is used to respond to the user input from the initial window selected from the test/sampling plan. If the user requests printing of the acceptance limit table or evaluation of a table, then the macro *caldisp2* is called. If the user requests a printout of the acceptance limit table, the macro *PRTDISP2* is called. If an evaluation is requested, the macro *EVDISP2* is called. After the evaluation macro is finished, the dataset SAVES2E is deleted. Finally, if the user requests a lower bound for a sample mean and standard deviation, the macro *SMPDISP2* is called.

APPENDIX G

TEST DATA

Content Uniformity
Sampling Plan 1
Test Data Set & Results

Target	CI Level	Lower Bound	Sample Size	Sample Mean	Program Result CV	Independent Result CV	Agree? (Y or N)
100	50.0	50.0	5	85.1			
				100.0			
				114.9			
			2000	85.1			
				100.0			
				114.9			
	99.0	50.0	5	85.1			
				100.0			
				114.9			
			2000	85.1			
				100.0			
				114.9			
	99.0	99.0	5	85.1			
				100.0			
				114.9			
			2000	85.1			
				100.0			
				114.9			
104.5	50.0	50.0	5	85.1			
				100.0			
				114.9			
			2000	85.1			
				100.0			
				114.9			
	50.0	99.0	5	85.1			
				100.0			
				114.9			
			2000	85.1			
				100.0			
				114.9			
	99.0	99.0	5	85.1			
				100.0			
				114.9			
			2000	85.1			
				100.0			
				114.9			

Content Uniformity
Sampling Plan 2
Test Data Set & Results

							Program	Independent	Program	Independent	All
Target	CI	Lower	# Loc	#/Location	SE	SM	Result	Result	Result	Result	Agree?
	Level	Bound					Mean	Mean	Mean	Mean	(Y or N)
							(Lower)	(Lower)	(Upper)	(Upper)	
100	50.0	50.0	3	2	0.1	0.1					
					0.1	3.0					
					3.0	0.1					
					3.0	3.0					
				300	0.1	0.1					
					0.1	3.0					
					3.0	0.1					
					3.0	3.0					
	50.0	99.0	300	2	0.1	0.1					
					0.1	3.0					
					3.0	0.1					
					3.0	3.0					
				300	0.1	0.1					
					0.1	3.0					
					3.0	0.1					
					3.0	3.0					
	99.0	99.0	3	2	0.1	0.1					
					3.0	3.0					
				300	0.1	0.1					
					0.1	3.0					
					3.0	0.1					
					3.0	3.0					
			300	300	0.1	0.1					
					0.1	3.0					
					3.0	0.1					
					3.0	3.0					
102.5	50.0	50.0	3	2	0.1	3.0					
	99.0	50.0	300	300	3.0	3.0					
	99.0	50.0	3	2	0.1	0.1					
				300	0.1	3.0					

ACCEPTANCE LIMITS FOR DISSOLUTION (N = 3, Q = 85.0)
 SAMPLING PLAN 1
 (MEETING LIMITS GUARANTEES WITH 50.0 % ASSURANCE,
 THAT AT LEAST 50.0% OF ALL FUTURE SAMPLES TESTED
 FOR DISSOLUTION WILL PASS THE USP TEST)
 TABLE ENTRY IS UPPER LIMIT ON CV OF 3 DISSOLUTION ASSAYS

MEAN (% CLAIM)	CV (%)	MEAN (% CLAIM)	CV (%)	MEAN (% CLAIM)	CV (%)	MEAN (% CLAIM)	CV (%)	MEAN (% CLAIM)	CV (%)
85.2	0.44	88.2	5.84	91.2	7.62	94.2	8.73	97.2	9.51
85.4	0.88	88.4	6.01	91.4	7.71	94.4	8.79	97.4	9.56
85.6	1.31	88.6	6.16	91.6	7.80	94.6	8.85	97.6	9.60
85.8	1.74	88.8	6.30	91.8	7.88	94.8	8.90	97.8	9.65
86.0	2.18	89.0	6.44	92.0	7.96	95.0	8.96	98.0	9.69
86.2	2.60	89.2	6.57	92.2	8.04	95.2	9.01	98.2	9.74
86.4	3.03	89.4	6.69	92.4	8.12	95.4	9.07	98.4	9.78
86.6	3.46	89.6	6.81	92.6	8.19	95.6	9.12	98.6	9.82
86.8	3.88	89.8	6.92	92.8	8.26	95.8	9.17	98.8	9.86
87.0	4.29	90.0	7.03	93.0	8.33	96.0	9.23	99.0	9.90
87.2	4.66	90.2	7.14	93.2	8.40	96.2	9.28	99.2	9.94
87.4	4.97	90.4	7.24	93.4	8.47	96.4	9.32	99.4	9.98
87.6	5.24	90.6	7.34	93.6	8.54	96.6	9.37	99.6	10.03
87.8	5.46	90.8	7.44	93.8	8.60	96.8	9.42	99.8	10.06
88.0	5.66	91.0	7.53	94.0	8.67	97.0	9.47	100.0	10.10

ACCEPTANCE LIMITS FOR DISSOLUTION (Q = 40.0)
SAMPLING PLAN 2
LOWER BOUND = 50.0, CONFIDENCE LEVEL = 99.0
TABLE ENTRIES ARE LOWER LIMITS ON THE MEAN
OF 6 ASSAYS- 2 ASSAYS AT EACH OF 3 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
SE								
0.25	45.30	50.60	57.30	66.00	76.70	88.10	99.70	
0.50	45.30	50.60	57.30	66.00	76.70	88.10	99.70	
0.75	45.30	50.60	57.30	66.00	76.70	88.10	99.70	
1.00	45.30	50.60	57.30	66.10	76.70	88.10	99.70	
1.25	45.30	50.70	57.40	66.20	76.80	88.20	99.80	
1.50	45.30	50.80	57.60	66.30	76.90	88.20	99.80	
1.75	45.50	51.10	57.90	66.50	77.00	88.30	99.90	
2.00	45.90	51.60	58.30	66.80	77.30	88.50	100.00	
2.25	46.60	52.20	58.90	67.30	77.60	88.70		
2.50	47.50	53.00	59.60	67.90	78.00	89.00		
2.75	48.50	54.10	60.60	68.70	78.50	89.30		
3.00	49.80	55.30	61.70	69.70	79.20	89.80		
3.25	51.30	56.80	63.10	70.80	80.00	90.30		
3.50	53.00	58.50	64.70	72.10	81.00	91.00		

3.75	54.90	60.30	66.40	73.60	82.10	91.80
4.00	56.80	62.20	68.20	75.10	83.30	92.70
4.25	58.80	64.20	70.00	76.70	84.60	93.70
4.50	60.80	66.20	71.90	78.50	86.10	94.80
4.75	62.80	68.20	73.90	80.30	87.60	96.10
5.00	64.90	70.20	75.90	82.10	89.20	97.40
5.25	67.00	72.30	77.90	84.00	90.90	98.80
5.50	69.10	74.40	79.90	85.90	92.70	
5.75	71.20	76.50	82.00	87.90	94.50	
6.00	73.30	78.60	84.00	89.90	96.30	
6.25	75.40	80.70	86.10	91.90	98.20	

J

(Continued)

ACCEPTANCE LIMITS FOR DISSOLUTION (Q = 40.0)
 SAMPLING PLAN 2
 LOWER BOUND = 50.0, CONFIDENCE LEVEL = 99.0
 TABLE ENTRIES ARE LOWER LIMITS ON THE MEAN
 OF 6 ASSAYS- 2 ASSAYS AT EACH OF 3 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
SE								
6.50	77.50	82.80	88.20	93.80	99.90			
6.75	79.30	84.60	90.00	95.60				
7.00	81.10	86.40	91.70	97.30				
7.25	82.90	88.20	93.50	99.10				
7.50	84.70	90.00	95.30					
7.75	86.50	91.80	97.10					
8.00	88.40	93.60	98.90					
8.25	90.20	95.40						
8.50	92.00	97.20						
8.75	93.80	99.10						
9.00	95.60							
9.25	97.40							
9.50	99.20							

FORMS

FORM 1
LOAD AND RUN PROGRAM

Name: Merlin Utter

Computer Description:

PC

Manufacturer: Hewlett Packard HP Company
Model: HC 6220
CPU Speed: 1.73 GHz
Hard Drive Size: 37.2 GB
RAM Memory: 503 Mb

SAS Version Number: 9.1

Sign below to indicate that the program, CuDAL, loaded and ran successfully on your PC.

Name Merlin Utter

Date: 10/19/2007

FORM 1
LOAD AND RUN PROGRAM

Name: Merlin Utter

Computer Description:

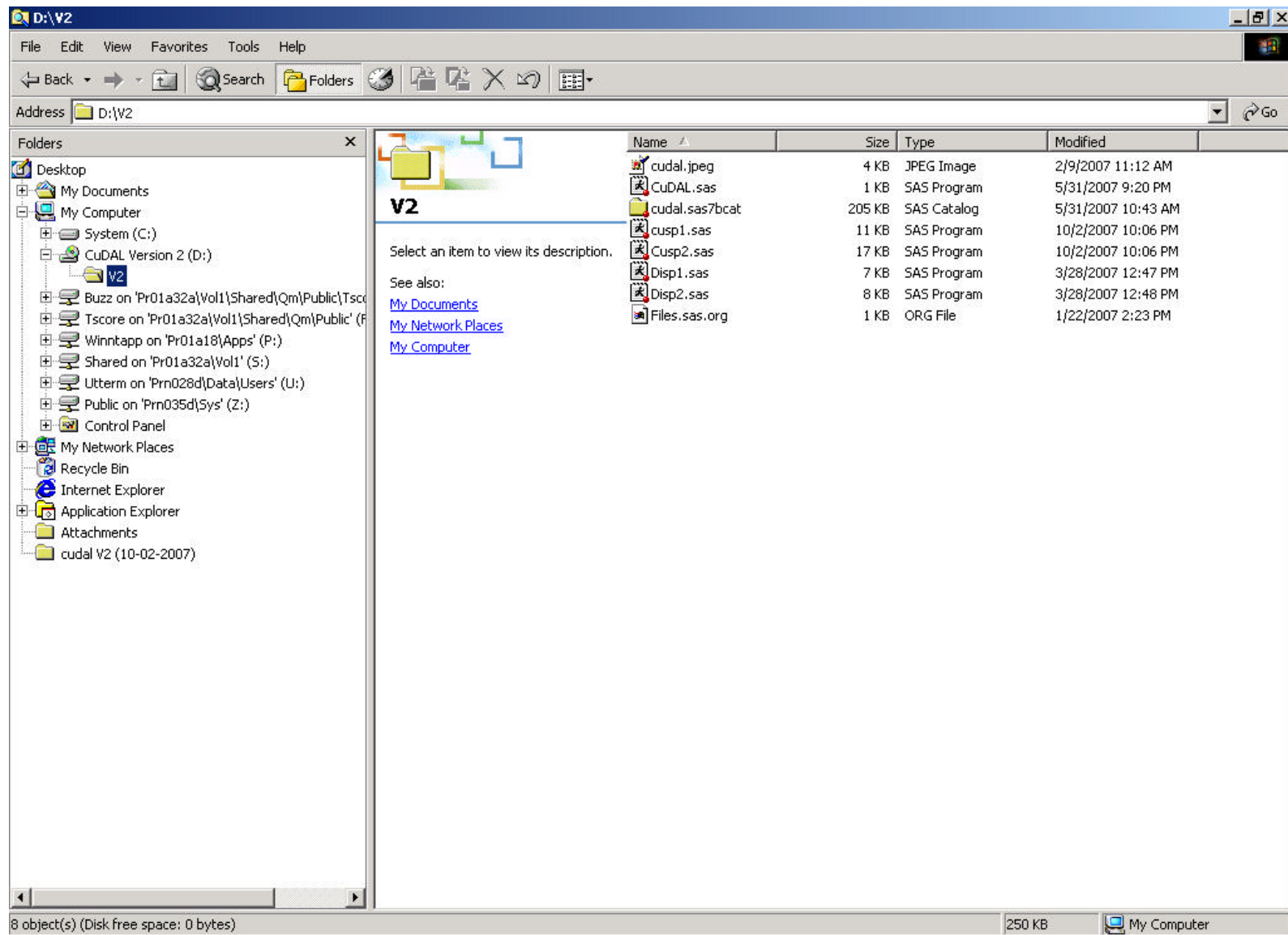
PC

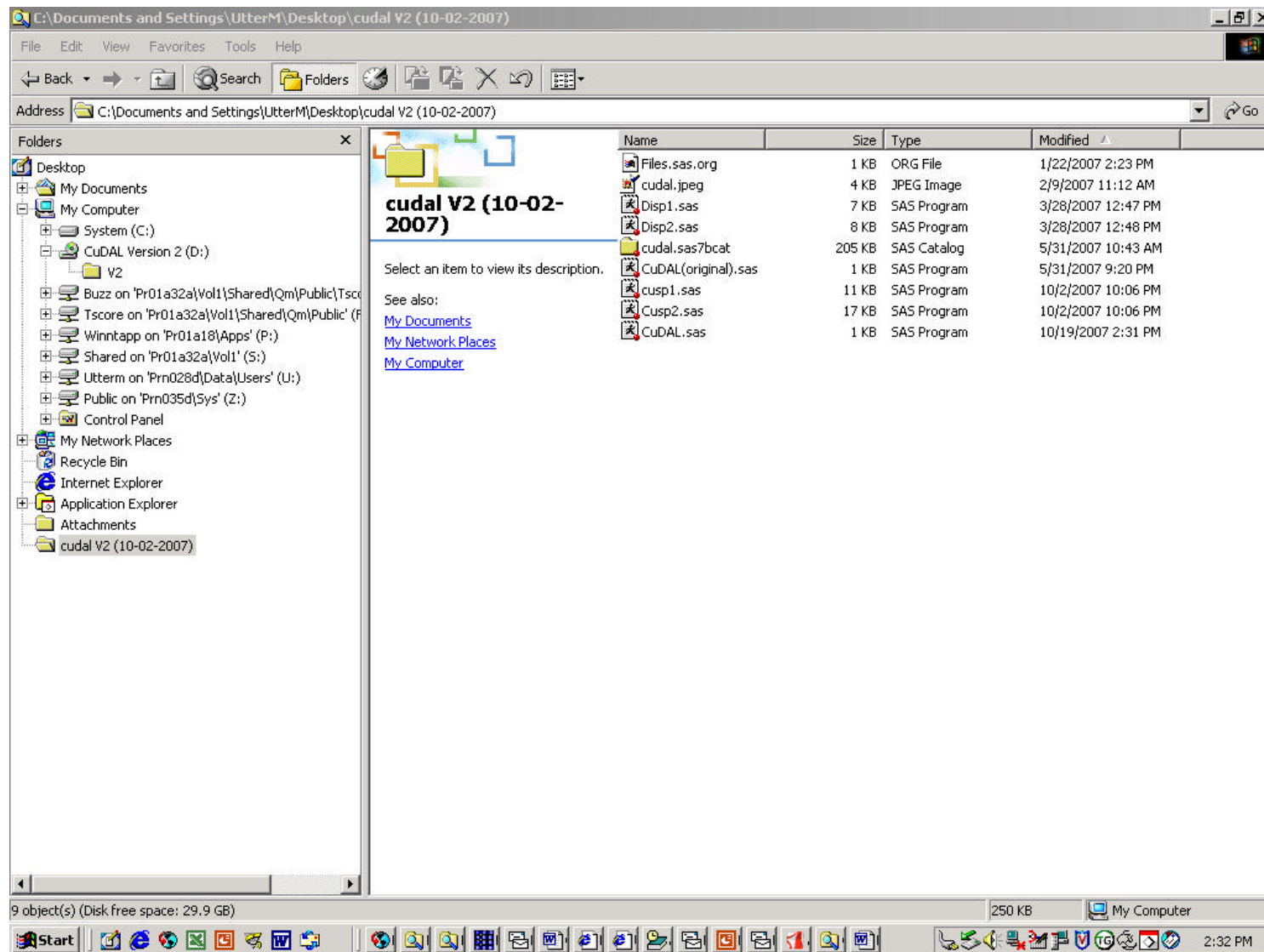
Manufacturer: Hewlett Packard HP Company
Model: HC 6220
CPU Speed: 1.73 GHz
Hard Drive Size: 37.2 GB
RAM Memory: 503 Mb

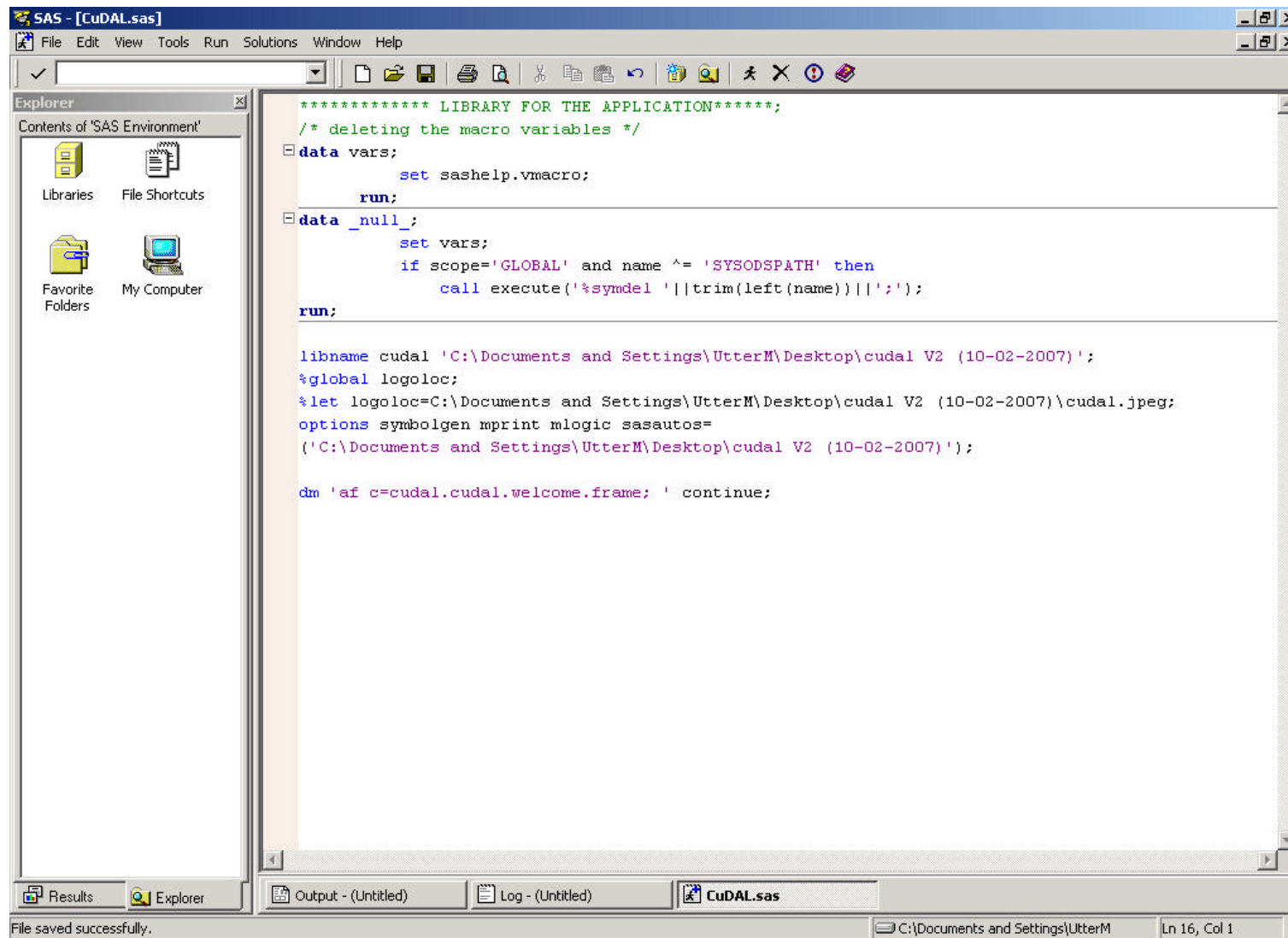
SAS Version Number: 9.1

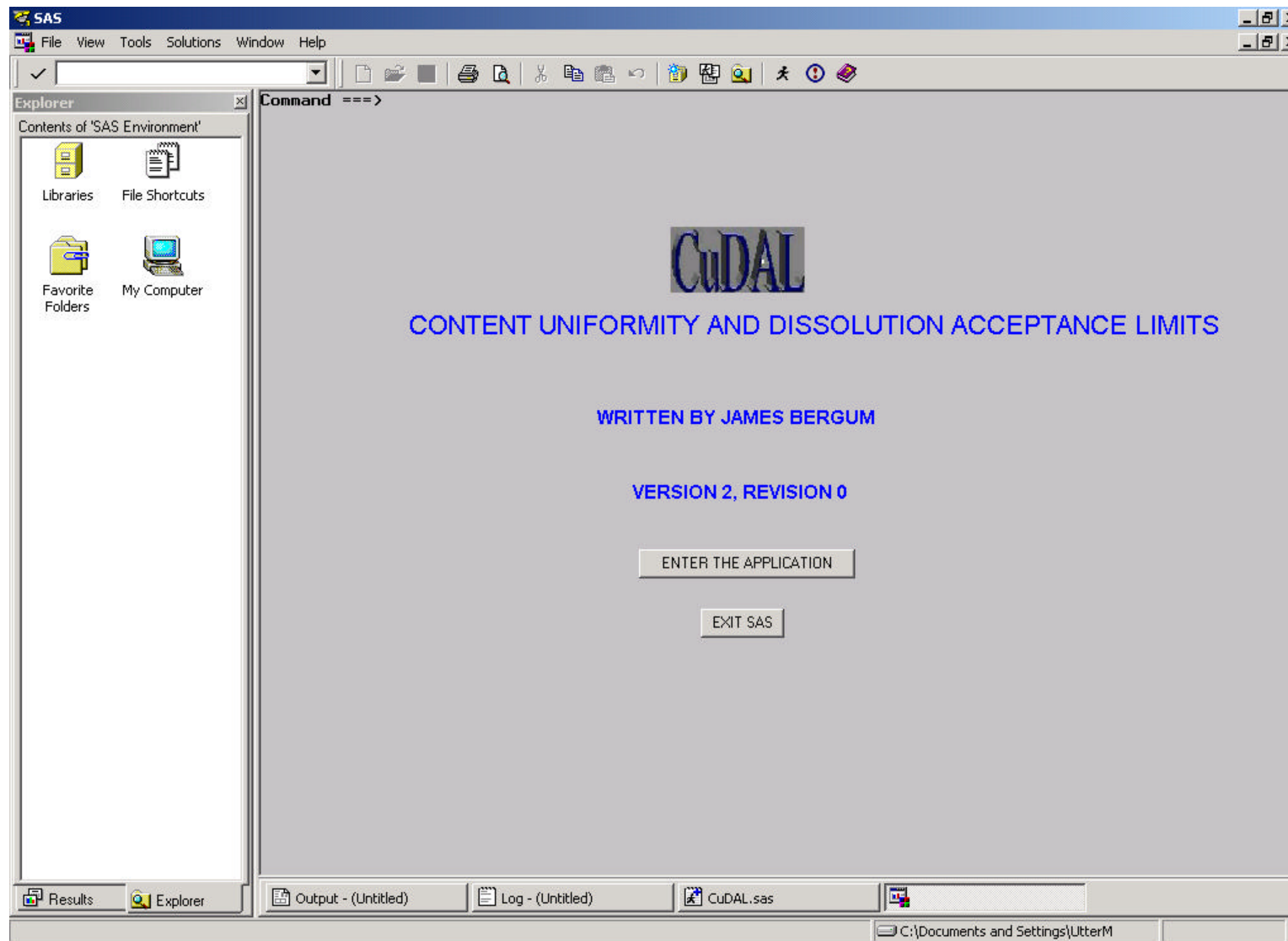
Sign below to indicate that the program, CuDAL, loaded and ran successfully on your PC.

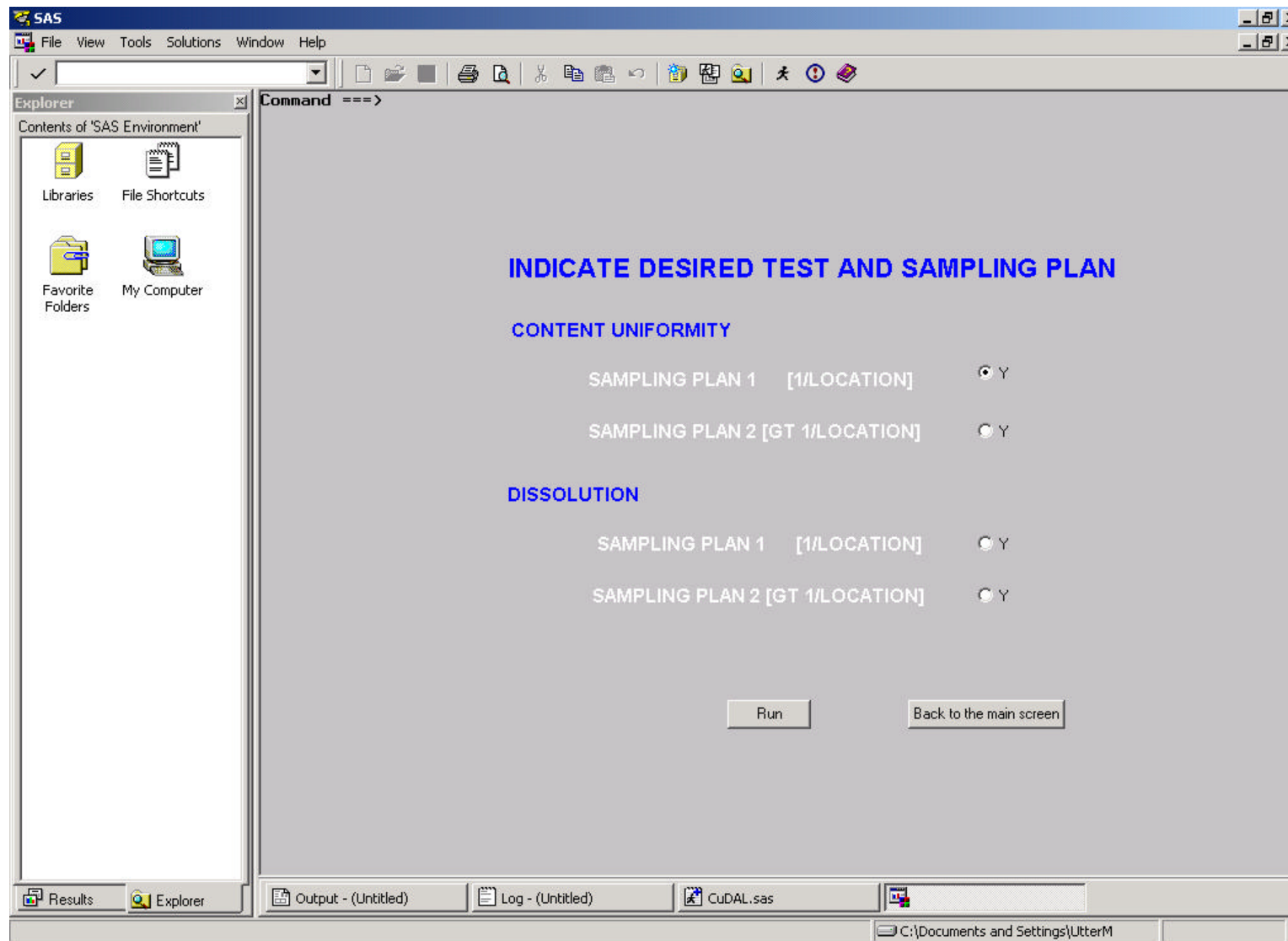
Name Merlin Utter Date: 7/25/2007











FORM 1

LOAD AND RUN PROGRAM

Name: Yigie Dang

Computer Description:

PC

Manufacturer: Lenovo
Model: 8808-W3V
CPU Speed: Intel Core 2 CPU 6200 @ 1.86 GHz
Hard Drive Size: 80 GB
RAM Memory: 1 GB

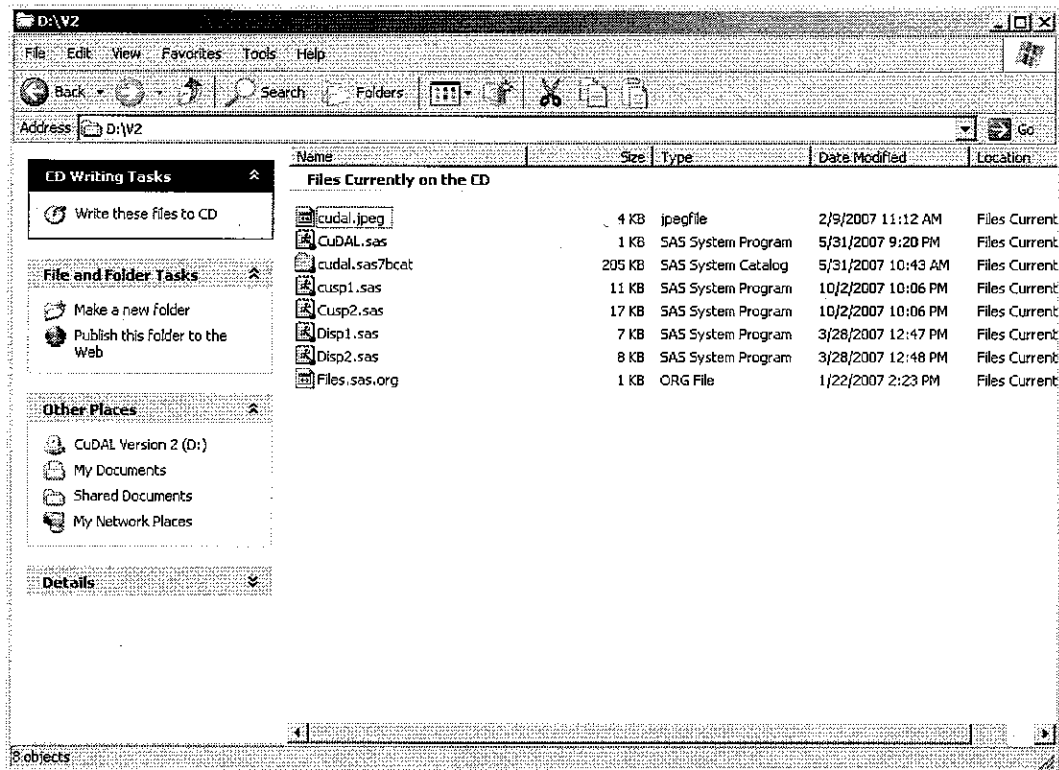
SAS Version Number: 8.2

Sign below to indicate that the program, CuDAL, loaded and ran successfully on your PC.

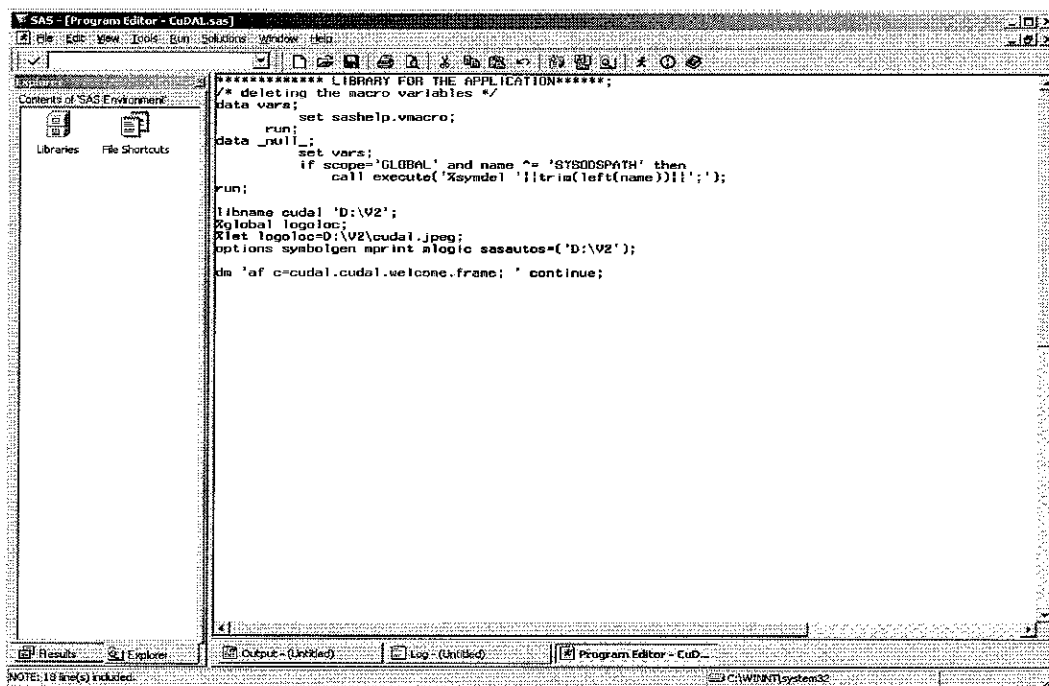
Name

Yigie Dang

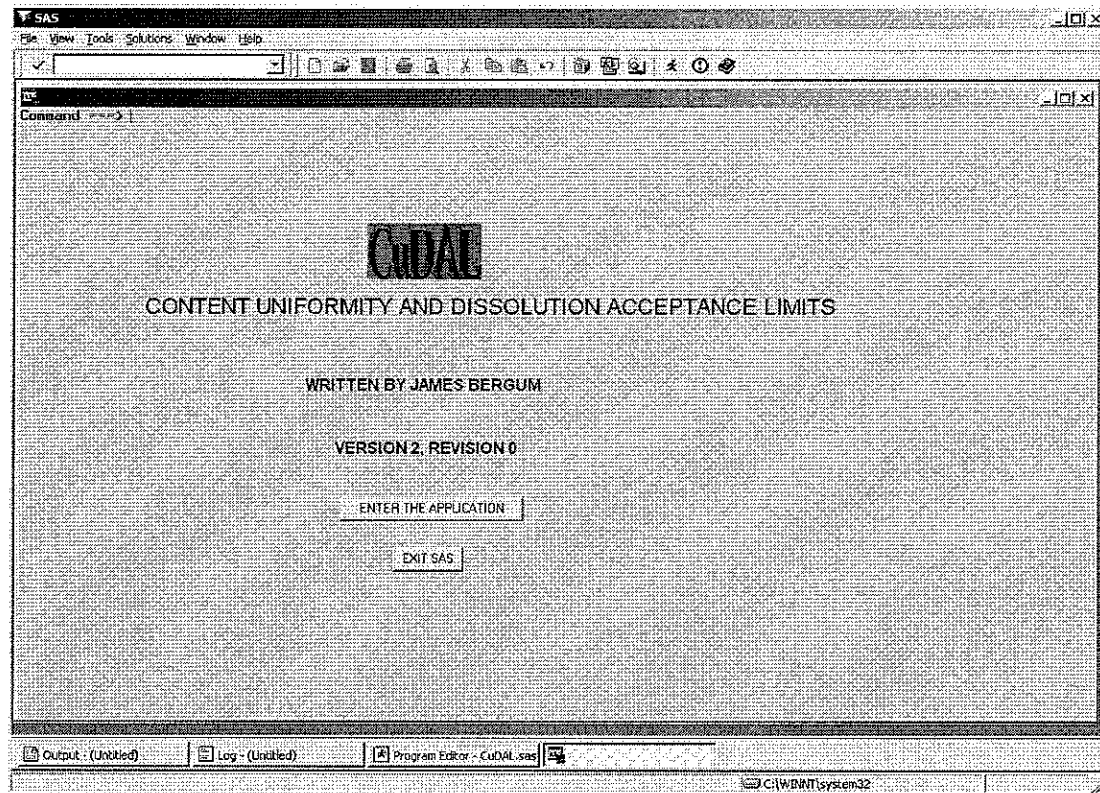
Date: Oct. 17, 2007



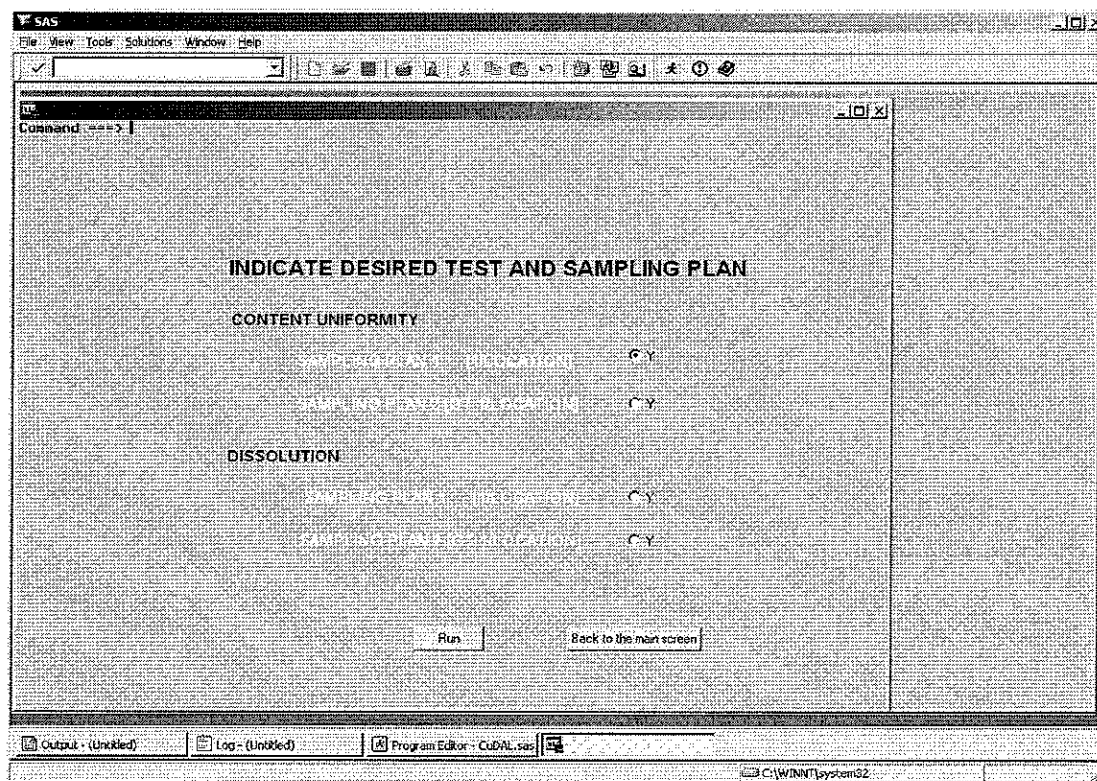
YD 10/17/2007



YD. 10/17/2007



YD Oct. 17, 2007



YD Oct. 17, 2007

FORM 1
LOAD AND RUN PROGRAM

Name: Myron Diener

Computer Description:

PC

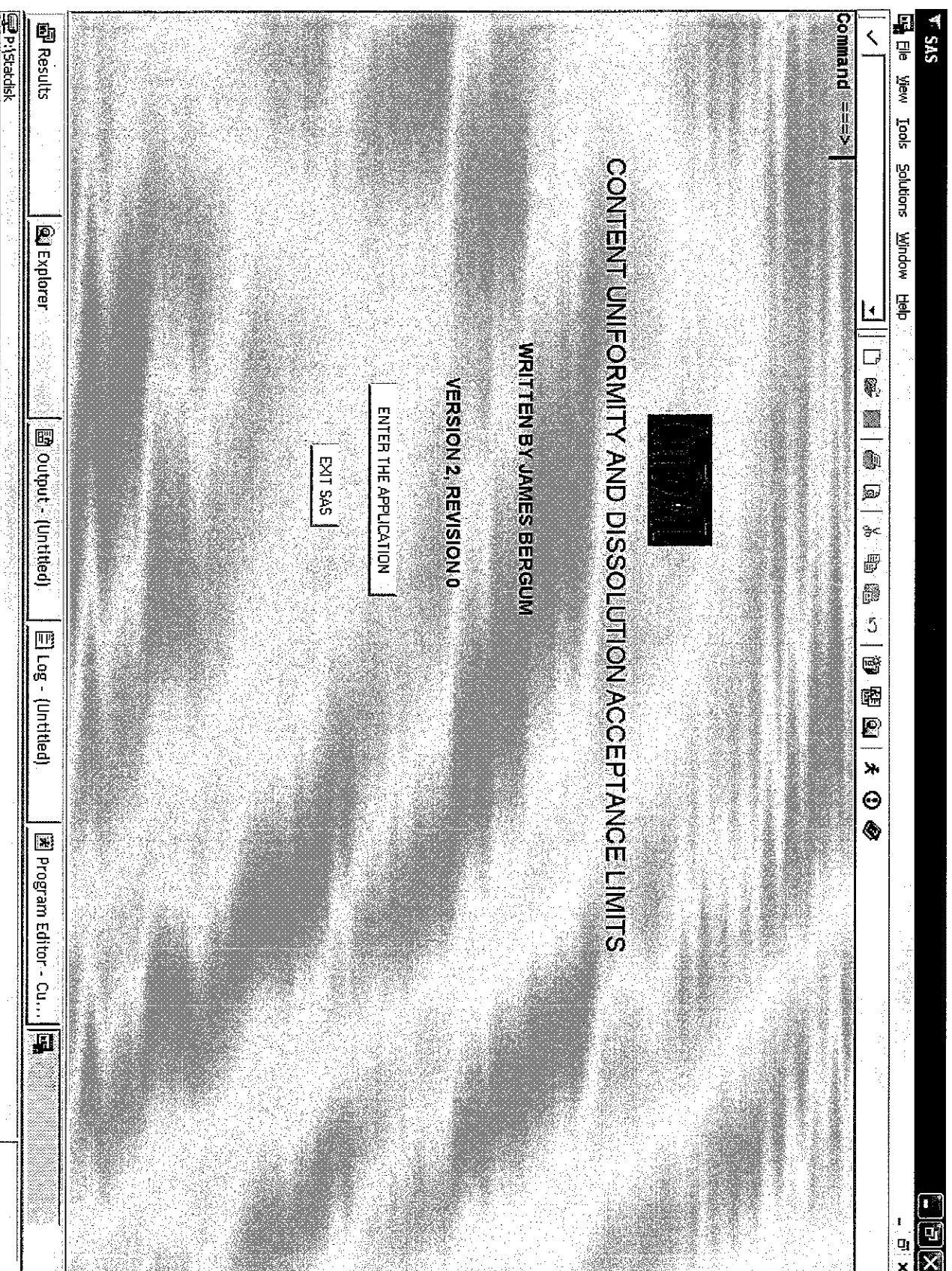
Manufacturer: IBM
Model: T42
CPU Speed: 1.70 GHz
Hard Drive Size: 37.2 GB
RAM Memory: 512 MB

SAS Version Number: 8.02

Sign below to indicate that the program, CuDAL, loaded and ran successfully on your PC.

Name Myron Diener Date: 10/18/07

Attached are screen shots of first and second screens.



SAS

File View Tools Solutions Window Help

Command

INDICATE DESIRED TEST AND SAMPLING PLAN

CONTENT UNIFORMITY

SAMPLING PLAN	ALLOCATION	CY
SAMPLING PLAN 1	ALLOCATION	CY
SAMPLING PLAN 2	ALLOCATION	CY

DISSOLUTION

SAMPLING PLAN 1	ALLOCATION	CY
SAMPLING PLAN 2	ALLOCATION	CY

Run

Back to the main screen

Results Explorer Output - (Untitled) Log - (Untitled) Program Editor - Cu...

FORM 1
LOAD AND RUN PROGRAM

Name: Myron Diener

Computer Description:

PC

Manufacturer:	<u>IBM</u>
Model:	<u>T42</u>
CPU Speed:	<u>1.70 GHz</u>
Hard Drive Size:	<u>40 GB</u>
RAM Memory:	<u>512 MB</u>

SAS Version Number: 8.02

Sign below to indicate that the program, CuDAL, loaded and ran successfully on your PC.

Name Myron Diener Date: 9/4/07

FORM 1

LOAD AND RUN PROGRAM

Name: Yijie Deng

Computer Description:

PC

Manufacturer: Lenovo 8808W3V
Model: Intel Core 2 / Windows XP 2002
CPU Speed: 6200 @ 1.86 GHz
Hard Drive Size: 80 GB
RAM Memory: 1 GB

SAS Version Number: 8.2

Sign below to indicate that the program, CuDAL, loaded and ran successfully on your PC.

Name

Yijie Deng

Date: 09/05/2007

FORM 1
LOAD AND RUN PROGRAM

Name: James Pazdan

Computer Description:

PC

Manufacturer: Compaq
Model: D507
CPU Speed: 1.996Hz
Hard Drive Size: 40GB
RAM Memory: 504MB

SAS Version Number: 8.2

Sign below to indicate that the program, CuDAL, loaded and ran successfully on your PC.

Name JP

Date: 7/27/07

FORM 1
LOAD AND RUN PROGRAM

Name: ROWLAND A. YOVONIE

Computer Description:

PC

Manufacturer:

COMPAQ

Model:

NOVO C

CPU Speed:

1.8 GHz Pentium 4M

Hard Drive Size:

5400

RAM Memory:

256 MBYTE

SAS Version Number:

8e for Windows

Sign below to indicate that the program, CuDAL, loaded and ran successfully on your PC.

Name

Rowland A. Yovonie

Date:

8/6/2007

FORM 1
LOAD AND RUN PROGRAM

Name: EDITH SENDERAK

Computer Description:

PC

Manufacturer:	<u>IBM</u>
Model:	<u>T2300</u>
CPU Speed:	<u>1.66 GHz</u>
Hard Drive Size:	<u>372GB</u>
RAM Memory:	<u>1 GB</u>

SAS Version Number: 9.1

Sign below to indicate that the program, CuDAL, loaded and ran successfully on your PC.

Name Edith Senderak Date: Aug. 2, 2007

FORM 1
LOAD AND RUN PROGRAM

Name: Dave LeBlond

Computer Description:

PC

Manufacturer: DELL
Model: Latitude C610
CPU Speed: 1.86 GHz
Hard Drive Size: 60 GByte
RAM Memory: 1 GByte

SAS Version Number: 8.02 TS02MO running under Windows
2006 5.00.2195 SP4

Sign below to indicate that the program, CuDAL, loaded and ran successfully on your PC.

Name

Dave LeBlond

Date:

7-26-07

FORM 1

LOAD AND RUN PROGRAM

Name: Stan Altan

Computer Description:

PC

Manufacturer: IBM

Model: ThinkCentre Desktop

CPU Speed: 3.00 GHz

Hard Drive Size: 37.2 GB

RAM Memory: 512 Mb

SAS Version Number: 9.1

Sign below to indicate that the program, CuDAL, loaded and ran successfully on your PC.

Name



Date: August 4, 2007

FORM 1

LOAD AND RUN PROGRAM

Name: Yijie Dang

Computer Description:

PC

Manufacturer: LENOVO
Model: 8808 W3V
CPU Speed: 6300 @ 1.86 GHZ (Intel Core 2 CPU)
Hard Drive Size: 80 GB
RAM Memory: 1 GB

SAS Version Number: 8.2

Sign below to indicate that the program, CuDAL, loaded and ran successfully on your PC.

Name

Yijie Dang
Yijie Dang

Date: June 22, 2007

FORM 1
LOAD AND RUN PROGRAM

Name: Brent Harrington

Computer Description:

PC

Manufacturer:	<u>hp</u>
Model:	<u>Compaq dc7100</u>
CPU Speed:	<u>3 GHz</u>
Hard Drive Size:	<u>40 GB</u>
RAM Memory:	<u>1 GB</u>

SAS Version Number: 9.1 for windows

Sign below to indicate that the program, CuDAL, loaded and ran successfully on your PC.

Name Bat/H/C

Date: 25 July 2007

FORM 2
PRIMARY WINDOW NAVIGATION
& INPUT ERROR CHECKS

Sign below to indicate that all of the found responses agree with the expected results in Appendix D.

Name: Myron Dines Date: 9/25/07

Navigation & Window Input Error Checking Lead

APPENDIX D NAVIGATION & ERROR CHECKS

Navigation (See Appendix B for window displays and names):

Test	Window	Instruction	Expected Result	Found Result	Agree (Y or N)
1	Opening Window	'Exit SAS'	Exit's SAS	✓	Y
2	Opening Window	'Enter the Application'	Opens Test/Sampling Plan Selection Window	✓	Y
	Test/Sampling Plan Selection Window	Select Content Uniformity - Sampling Plan 1	Opens Initial Content Uniformity Sampling Plan 1 Window	✓	Y
	Initial Content Uniformity Sampling Plan 1 Window	Select 'Cancel'	Returns to Test/Sampling Plan Selection Window	✓	Y
	Test/Sampling Plan Selection Window	Select Content Uniformity - Sampling Plan 1	Opens Initial Content Uniformity Sampling Plan 1 Window	✓	Y
	Initial Content Uniformity Sampling Plan 1 Window	Select Yes to Print Table, Evaluate Table, and Find Lower Bound for a sample result. Select 'Run'	Opens Evaluation Sub-Window	✓	Y
	Evaluation Sub-Window	Select 'Run'	Opens Lower Bound for Sample Result Sub-Window	✓	Y
	Sample Result Sub-Window	Select 'Run'	Returns to Initial Content Uniformity Sampling Plan 1 Window	then output window	Y
	Initial Content Uniformity Sampling Plan 1 Window	Select 'Cancel'	Returns to Test/Sampling Plan Selection Window	✓	Y
	Test/Sampling Plan Selection Window	Select 'Cancel' back to main screen	Returns to Opening Window	✓	Y
3	Opening Window	Select 'Enter the Application', Select Content Uniformity - Sampling Plan 2	Opens Initial Content Uniformity Sampling Plan 2 Window	✓	Y
	Initial Content Uniformity Sampling Plan 2 Window	Select 'Cancel'	Returns to Test/Sampling Plan Selection Window	✓	Y
	Test/Sampling Plan Selection Window	Select Content Uniformity - Sampling Plan 2	Opens Initial Content Uniformity Sampling Plan 2 Window	✓	Y
	Initial Content Uniformity Sampling Plan 2 Window	Select Yes to Print Table, Evaluate Table, and Find Lower Bound for a sample result. Select 'Run'	Opens Evaluation Sub-Window	✓	Y
	Evaluation Sub-Window	Select 'Run'	Opens Lower Bound for Sample Result Sub-Window	✓	Y
	Sample Result Sub-Window	Select 'Run'	Returns to Initial Content Uniformity	✓	Y

			Sampling Plan 2 Window	<i>then Output Window</i>	
	Initial Content Uniformity Sampling Plan 2 Window	Select 'Cancel'	Returns to Test/Sampling Plan Selection Window	✓	Y
	Test/Sampling Plan Selection Window	Select 'Cancel'	Returns to Opening Window	✓	Y
4	Opening Window	<i>Back to Main Screen</i> Select 'Enter the Application', Select Dissolution - Sampling Plan 1	Opens Initial Dissolution - Sampling Plan 1 Window	✓	Y
	Initial Dissolution Sampling Plan 1 Window	Select 'Cancel'	Returns to Test/Sampling Plan Selection Window	✓	Y
	Test/Sampling Plan Selection Window	Select Dissolution - Sampling Plan 1	Opens Initial Dissolution Sampling Plan 1 Window	✓	Y
	Initial Dissolution Sampling Plan 1 Window	Select Yes to Print Table, Evaluate Table, and Find Lower Bound for a sample result. Select 'Run'	Opens Evaluation Sub-Window	✓	Y
	Evaluation Sub-Window	Select 'Run'	Opens Lower Bound for Sample Result Sub-Window	✓	Y
	Sample Result Sub-Window	Select 'Run'	Returns to Initial Dissolution Sampling Plan 1 Window	<i>then Output Window</i>	Y
	Initial Dissolution Sampling Plan 1 Window	Select 'Cancel'	Returns to Test/Sampling Plan Selection Window	✓	Y
	Test/Sampling Plan Selection Window	Select 'Cancel'	Returns to Opening Window	✓	Y
5	Opening Window	<i>Back to main screen</i> Select 'Enter the Application', Select Dissolution - Sampling Plan 2	Opens Initial Dissolution Sampling Plan 2 Window	✓	Y
	Initial Dissolution Sampling Plan 2 Window	Select 'Cancel'	Returns to Test/Sampling Plan Selection Window	✓	Y
	Test/Sampling Plan Selection Window	Select Dissolution - Sampling Plan 2	Opens Initial Dissolution Sampling Plan 2 Window	✓	Y
	Initial Dissolution Sampling Plan 2 Window	Select Yes to Print Table, Evaluate Table, and Find Lower Bound for a sample result. Select 'Run'	Opens Evaluation Sub-Window	✓	Y
	Evaluation Sub-Window	Select 'Run'	Opens Lower Bound for Sample Result Sub-Window	✓	Y
	Sample Result Sub-Window	Select 'Run'	Returns to Initial Dissolution Sampling Plan 2 Window	<i>then Output Window</i>	Y
	Initial Dissolution Sampling Plan 1 Window	Select 'Cancel'	Returns to Test/Sampling Plan Selection Window	✓	Y
	Test/Sampling Plan Selection Window	Select 'Cancel'	Returns to Opening Window	✓	Y
		<i>Back to Main Screen</i>			

**APPENDIX D
WINDOW INPUT ERROR CHECKING
TEST DATA**

**CONTENT UNIFORMITY
SAMPLING PLAN 1**

Window	Requested Input	User Input	EXPECTED RESPONSE	FOUND RESPONSE	AGREE? (Y or N)
			N = NONE	N or ES	
			ES = ERROR SCREEN		
Initial Window	Sample Size	5	N	N	Y
		4	ES	ES	Y
		2000	N	N	Y
	Bound	50	N	N	Y
		99	N	N	Y
		49.9	ES	ES	Y
		99.1	ES	ES	Y
		75	N	N	Y
	Confidence Interval	50	N	N	Y
		99	N	N	Y
		49.9	ES	ES	Y
		99.1	ES	ES	Y
		65	N	N	Y
Evaluate Sub Window	Lower Bound Mean	0	ES	ES	Y
	Upper Bound Mean	0	ES	ES	Y
	Increment Mean	0	ES	ES	Y
	Lower Bound CV	0	ES	ES	Y
	Upper Bound CV	0	ES	ES	Y
	Increment CV	0	ES	ES	Y
Lower Bound Based on Sample Result	Sample Mean	85.1	N	N	Y
		114.9	N	N	Y
		85	ES	ES	Y
		115	ES	ES	Y
	Sample CV	100.123	N	N	Y
		0.1	N	N	Y
		0	ES	ES	Y
		15	N	N	Y
		-3	ES	ES	Y

**CONTENT UNIFORMITY
SAMPLING PLAN 2**

Window	Requested Input	User Input	EXPECTED RESPONSE	FOUND RESPONSE	AGREE? (Y or N)
			N = NONE	N or ES	
			ES = ERROR SCREEN		
Initial Window	Number of Locations	3	N	N	Y
		2	ES	ES	
		2000	N	N	
	Number per location	2	N	N	
		1	ES	ES	
		2000	N	N	
	Bound	50	N	N	
		99	N	N	
		49.9	ES	ES	
	Confidence Level	99.1	ES	ES	
		80	N	N	
		50	N	N	
		99	N	N	
		49.9	ES	ES	
		99.1	ES	ES	
		70	N	N	
Evaluate Sub-Window	Lower Bound Mean	0	ES	ES	Y
	Upper Bound Mean	0	ES	ES	
	Increment Mean	0	ES	ES	
	Lower Bound Within SD	0	ES	ES	
	Upper Bound Within SD	0	ES	ES	
	Increment Within SD	0	ES	ES	
	Lower Bound Between SD	0	ES	ES	
	Upper Bound Between SD	0	ES	ES	
Lower Bound Based on Sample Result	Sample Mean	85.1	N	N	Y
		114.9	N	N	
		85	ES	ES	
		115	ES	ES	
		100.123	N	N	
	Sample Within SD	0.1	N	N	
		0	ES	ES	
		15	N	N	
		-3	ES	ES	
		0.1	N	N	
	Sample Between SD	0	ES	ES	
		15	N	N	
		-3	ES	ES	

**DISSOLUTION
SAMPLING PLAN 1**

Window	Requested Input	User Input	EXPECTED RESPONSE	FOUND RESPONSE	AGREE? (Y or N)
			N = NONE	N or ES	
			ES = ERROR SCREEN		
Initial Window	Q	40	N	N	Y
		95	N	N	Y
		39.9	ES	ES	Y
		95.1	ES	ES	Y
	Sample Size	3	N	N	Y
		2	ES	ES	Y
		2000	N	N	Y
	Bound	50	N	N	Y
		99	N	N	Y
		49.9	ES	ES	Y
		99.1	ES	ES	Y
		75	N	N	Y
	Confidence Level	50	N	N	Y
		99	N	N	Y
		49.9	ES	ES	Y
		99.1	ES	ES	Y
		80	N	N	Y
Evaluate Sub Window	Lower Bound Mean	0	ES	ES	Y
	Upper Bound Mean	0	ES	ES	Y
	Increment Mean	0	ES	ES	Y
	Lower Bound CV	0	ES	ES	Y
	Upper Bound CV	0	ES	ES	Y
	Increment CV	0	ES	ES	Y
Lower Bound Based on Sample Result	Sample Mean	75.1	N	N	Y
	(Q = 75)	100	N	N	Y
		85.5	N	N	Y
		75	ES	N	N
	Sample CV	0.1	N	N	Y
		0	ES	ES	Y
		15	N	N	Y
		-3	ES	ES	Y

**DISSOLUTION
SAMPLING PLAN 2**

Window	Requested Input	User Input	EXPECTED RESPONSE	FOUND RESPONSE	AGREE? (Y or N)
			N = NONE	N or ES	
			ES = ERROR SCREEN		
Initial Window	Q	40	N	IV	Y
		95	N	IV	Y
		39.9	ES	ES	Y
		95.1	ES	ES	Y
	Number of Locations	3	N	IV	Y
		2	ES	ES	Y
		2000	N	IV	Y
	Number per Location	2	N	IV	Y
		1	ES	ES	Y
		2000	N	N	Y
	Bound	50	N	N	Y
		99	N	N	Y
		49.9	ES	ES	Y
		99.1	ES	ES	Y
		65	N	N	Y
	Confidence Level	50	N	IV	Y
		99	N	N	Y
		49.9	ES	ES	Y
		99.1	ES	ES	Y
		80	N	IV	Y
Evaluate Sub-Window	Lower Bound Mean	0	ES	ES	Y
	Upper Bound Mean	0	ES	ES	Y
	Increment Mean	0	ES	ES	Y
	Lower Bound Within SD	0	ES	ES	Y
	Upper Bound Within SD	0	ES	ES	Y
	Increment Within SD	0	ES	ES	Y
	Lower Bound Between SD	0	ES	ES	Y
	Upper Bound Between SD	0	ES	ES	Y
	Increment Between SD	0	ES	ES	Y
Lower Bound Based on Sample Result	Sample Mean	60.1	N	N	Y
	(Q = 60)	100	N	N	Y
		80.6	N	IV	Y
		60	ES	N	IV
	Sample Within SD	0.1	N	IV	Y
		0	ES	ES	Y
		15	N	IV	Y
		-3	ES	ES	Y
	Sample Between SD	0.1	N	N	Y
		0	ES	ES	Y
		15	N	IV	Y
		-3	ES	ES	Y

**APPENDIX D
WINDOW INPUT ERROR
CHECKING
TEST DATA**

**DISSOLUTION
SAMPLING PLAN 1**

Window	Requested Input	User Input	EXPECTED RESPONSE	FOUND RESPONSE	AGREE? (Y or N)
			N = NONE	N or ES	
			ES = ERROR SCREEN		
Lower Bound Based on Sample Result	Sample Mean	75.1	N	N	Y
	(Q = 75)	100.1	ES	ES	Y
		85.5	N	N	Y
		74.9	ES	ES	Y

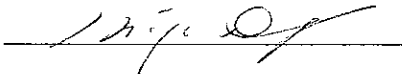
**DISSOLUTION
SAMPLING PLAN 2**

Window	Requested Input	User Input	EXPECTED RESPONSE	FOUND RESPONSE	AGREE? (Y or N)
			N = NONE	N or ES	
			ES = ERROR SCREEN		
Lower Bound Based on Sample Result	Sample Mean	60.1	N	N	Y
	(Q = 60)	100.1	ES	ES	Y
		80.6	N	N	Y
		59.9	ES	ES	Y

FORM 3

MATHEMATICAL CALCULATION VERIFICATION

Signing below indicates that the calculations described in Appendix E to determine lower bounds for content uniformity are correct.

Name:  Date: Sept. 24, 2007

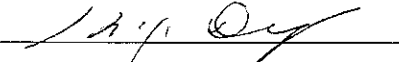
Macro Strategy, SAS Code & Mathematical Calculation Lead

FORM 4

PROGAM STRATEGY & SAS CODE VERIFICATION

Signing below indicates the following:

- 1) The calculations described in Appendix E to determine lower bounds for content uniformity and dissolution are implemented correctly in the macros.
- 2) The strategies described in Appendix F are appropriate.
- 3) The SAS code implements the strategies described in Appendix F correctly.

Name:  Date: Sept. 24, 2007

Macro Strategy, SAS Code & Mathematical Calculation Lead

FORM 5

TEST DATA SET AGREEMENT

Test Table generation

Signing below indicates that for the test data in Appendix G, CuDAL results agree with the results of independent calculations for content uniformity and are identical to the tables generated by version 1 for dissolution.

Name: Merlin Utter Date: 10/18/2007

Test Data Evaluation & Independent Calculations Lead

Exhibit 1.4 Checking Independent Results against Expected Results (Content Uniformity - Sampling Plan 1)

Sample Size	Target	Lower Bound	CI Level	Sample Mean	CUDAL CV	SPLUS Code CV	Agree? (Y/N)
5	100.0	50.0	50.0	85.1	0.56	0.56	Y
				100.0	4.88	4.87	N
				114.9	0.42	0.42	Y
2,000	100.0	50.0	50.0	85.1	0.93	0.93	Y
				100.0	7.31	7.31	Y
				114.9	0.69	0.69	Y
5	100.0	50.0	99.0	85.1	0.13	0.13	Y
				100.0	1.16	1.16	Y
				114.9	0.10	0.1	Y
2,000	100.0	50.0	99.0	85.1	0.88	0.88	Y
				100.0	7.06	7.06	Y
				114.9	0.65	0.65	Y
5	100.0	99.0	99.0	85.1	0.11	0.11	Y
				100.0	0.94	0.94	Y
				114.9	0.08	0.08	Y
2,000	100.0	99.0	99.0	85.1	0.64	0.64	Y
				100.0	5.41	5.41	Y
				114.9	0.48	0.48	Y
5	104.5	50.0	50.0	85.1	0.56	0.56	Y
				100.0	4.75	4.75	Y
				114.9	1.20	1.20	Y
2,000	104.5	50.0	50.0	85.1	0.93	0.93	Y
				100.0	7.21	7.21	Y
				114.9	1.98	1.98	Y
5	104.5	50.0	99.0	85.1	0.13	0.13	Y
				100.0	1.14	1.14	Y
				114.9	0.28	0.28	Y
2,000	104.5	50.0	99.0	85.1	0.88	0.88	Y
				100.0	6.94	6.94	Y
				114.9	1.88	1.88	Y
5	104.5	99.0	99.0	85.1	0.11	0.11	Y
				100.0	0.93	0.93	Y
				114.9	0.23	0.23	Y
2,000	104.5	99.0	99.0	85.1	0.64	0.64	Y
				100.0	5.29	5.29	Y
				114.9	1.37	1.37	Y

Exhibit 1.4 Checking Independent Results against Expected Results (Content Uniformity - Sampling Plan 2)

# Location	#/Location	Target	Lower Bound	CI Level	SE	SM	CUDAL's Mean		SPLUS Code's Mean		Agree? (Y/N)
							Lower Bound	Upper Bound	Lower Bound	Upper Bound	
3	2	100.0	50.0	50.0	0.1	0.1	84.8	115.2	84.8	115.2	Y
					0.1	3.0	96.8	103.2	96.8	103.2	Y
					3.0	0.1	89.8	110.2	89.8	110.2	Y
					3.0	3.0	97.8	102.2	97.8	102.2	Y
3	300	100.0	50.0	50.0	0.1	0.1	84.8	115.2	84.8	115.2	Y
					0.1	3.0	96.8	103.2	96.8	103.2	Y
					3.0	0.1	89.7	110.3	89.7	110.3	Y
					3.0	3.0	98.5	101.5	98.5	101.5	Y
300	2	100.0	50.0	50.0	0.1	0.1	84.8	115.2	84.8	115.2	Y
					0.1	3.0	89.8	110.2	89.8	110.2	Y
					3.0	0.1	87.9	112.1	87.9	112.1	Y
					3.0	3.0	91.1	108.9	91.1	108.9	Y
300	300	100.0	50.0	50.0	0.1	0.1	84.8	115.2	84.8	115.2	Y
					0.1	3.0	89.8	110.2	89.8	110.2	Y
					3.0	0.1	89.5	110.5	89.5	110.5	Y
					3.0	3.0	92.2	107.8	92.2	107.8	Y
3	2	100.0	99.0	50.0	0.1	0.1	84.8	115.2	84.8	115.2	Y
					0.1	3.0	NA	NA	NA	NA	Y
					3.0	0.1	92.2	107.8	92.2	107.8	Y
					3.0	3.0	NA	NA	NA	NA	Y
3	300	100.0	99.0	50.0	0.1	0.1	84.8	115.2	84.8	115.2	Y
					0.1	3.0	NA	NA	NA	NA	Y
					3.0	0.1	92.0	108.0	92.0	108.0	Y
					3.0	3.0	NA	NA	NA	NA	Y
300	2	100.0	99.0	50.0	0.1	0.1	84.8	115.2	84.8	115.2	Y
					0.1	3.0	92.2	107.8	92.2	107.8	Y
					3.0	0.1	89.5	110.5	89.5	110.5	Y
					3.0	3.0	94.0	106.0	94.0	106.0	Y
300	300	100.0	99.0	50.0	0.1	0.1	84.8	115.2	84.8	115.2	Y
					0.1	3.0	92.2	107.8	92.2	107.8	Y
					3.0	0.1	91.8	108.2	91.8	108.2	Y
					3.0	3.0	95.5	104.5	95.5	104.5	Y

# Location	#/Location	Target	Lower Bound	CI Level	SE	SM	CUDAL's Mean		SPLUS Code's Mean		Agree? (Y/N)
							Lower Bound	Upper Bound	Lower Bound	Upper Bound	
3	2	100.0	99.0	99.0	0.1	0.1	89.7	110.3	89.7	110.3	Y
					0.1	3.0	NA	NA	NA	NA	Y
					3.0	0.1	NA	NA	NA	NA	Y
3	300	100.0	99.0	99.0	3.0	3.0	NA	NA	NA	NA	Y
					0.1	0.1	89.7	110.3	89.7	110.3	Y
					0.1	3.0	NA	NA	NA	NA	Y
300	2	100.0	99.0	99.0	3.0	0.1	95.0	105.0	95.0	105.0	Y
					3.0	3.0	NA	NA	NA	NA	Y
					0.1	0.1	84.8	115.2	84.8	115.2	Y
300	300	100.0	99.0	99.0	0.1	3.0	93.3	106.7	93.3	106.7	Y
					3.0	0.1	90.1	109.9	90.1	109.9	Y
					3.0	3.0	95.1	104.9	95.1	104.9	Y
					0.1	0.1	84.8	115.2	84.8	115.2	Y
					0.1	3.0	93.3	106.7	93.3	106.7	Y
					3.0	0.1	91.8	108.2	91.8	108.2	Y
					3.0	3.0	96.4	103.6	96.4	103.6	Y
					0.1	3.0	96.8	104.2	96.8	104.2	Y
					3.0	3.0	93.0	108.0	93.0	108.0	Y
3	2	102.5	50.0	50.0	0.1	0.1	88.6	112.4	88.6	112.4	Y
300	300	102.5	50.0	99.0	0.1	3.0	NA	NA	NA	NA	Y
3	2	102.5	50.0	99.0	0.1	0.1	88.6	112.4	88.6	112.4	Y
3	300	102.5	50.0	99.0	0.1	3.0	NA	NA	NA	NA	Y

Note: highlighted test cases not included in the protocol.

ACCEPTANCE LIMITS FOR DISSOLUTION (N = 3, Q = 85.0)
SAMPLING PLAN 1

(MEETING LIMITS GUARANTEES WITH 50.0 % ASSURANCE,
THAT AT LEAST 50.0% OF ALL FUTURE SAMPLES TESTED

FOR DISSOLUTION WILL PASS THE USP TEST)

TABLE ENTRY IS UPPER LIMIT ON CV OF 3 DISSOLUTION ASSAYS

MEAN (% CLAIM)	CV (%)	MEAN (% CLAIM)	CV (%)	MEAN (% CLAIM)	CV (%)	MEAN (% CLAIM)	CV (%)	MEAN (% CLAIM)	CV (%)
85.2	0.44	88.2	5.84	91.2	7.62	94.2	8.73	97.2	9.51
85.4	0.88	88.4	6.01	91.4	7.71	94.4	8.79	97.4	9.56
85.6	1.31	88.6	6.16	91.6	7.80	94.6	8.85	97.6	9.60
85.8	1.74	88.8	6.30	91.8	7.88	94.8	8.90	97.8	9.65
86.0	2.18	89.0	6.44	92.0	7.96	95.0	8.96	98.0	9.69
86.2	2.60	89.2	6.57	92.2	8.04	95.2	9.01	98.2	9.74
86.4	3.03	89.4	6.69	92.4	8.12	95.4	9.07	98.4	9.78
86.6	3.46	89.6	6.81	92.6	8.19	95.6	9.12	98.6	9.82
86.8	3.88	89.8	6.92	92.8	8.26	95.8	9.17	98.8	9.86
87.0	4.29	90.0	7.03	93.0	8.33	96.0	9.23	99.0	9.90
87.2	4.66	90.2	7.14	93.2	8.40	96.2	9.28	99.2	9.94
87.4	4.97	90.4	7.24	93.4	8.47	96.4	9.32	99.4	9.98
87.6	5.24	90.6	7.34	93.6	8.54	96.6	9.37	99.6	10.03
87.8	5.46	90.8	7.44	93.8	8.60	96.8	9.42	99.8	10.06
88.0	5.66	91.0	7.53	94.0	8.67	97.0	9.47	100.0	10.10

Output of New Version
of CuDAL to be
Compared against
that in CuDAL Test
Plan. Checks next
to numbers indicate
the value is identical
to that in CuDAL test
Plan. *David Bell*
10-18-2007

ACCEPTANCE LIMITS FOR DISSOLUTION (Q = 40.0)
 SAMPLING PLAN 2
 LOWER BOUND = 50.0, CONFIDENCE LEVEL = 99.0
 TABLE ENTRIES ARE LOWER LIMITS ON THE MEAN
 OF 6 ASSAYS- 2 ASSAYS AT EACH OF 3 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		
0.25	45.30	50.60	57.30	66.00	76.70	88.10	99.70	.		
0.50	45.30	50.60	57.30	66.00	76.70	88.10	99.70	.		
0.75	45.30	50.60	57.30	66.00	76.70	88.10	99.70	.		
1.00	45.30	50.60	57.30	66.10	76.70	88.10	99.70	.		
1.25	45.30	50.70	57.40	66.20	76.80	88.20	99.80	.		
1.50	45.30	50.80	57.60	66.30	76.90	88.20	99.80	.		
1.75	45.50	51.10	57.90	66.50	77.00	88.30	99.90	.		
2.00	45.90	51.60	58.30	66.80	77.30	88.50	100.00	.		
2.25	46.60	52.20	58.90	67.30	77.60	88.70	.	.		
2.50	47.50	53.00	59.60	67.90	78.00	89.00	.	.		
2.75	48.50	54.10	60.60	68.70	78.50	89.30	.	.		

David B. B.
 10-18-07

(Continued)

ACCEPTANCE LIMITS FOR DISSOLUTION (Q = 40.0)
SAMPLING PLAN 2
LOWER BOUND = 50.0, CONFIDENCE LEVEL = 99.0
TABLE ENTRIES ARE LOWER LIMITS ON THE MEAN
OF 6 ASSAYS- 2 ASSAYS AT EACH OF 3 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		
3.00	49.80	55.30	61.70	69.70	79.20	89.80				
3.25	51.30	56.80	63.10	70.80	80.00	90.30				
3.50	53.00	58.50	64.70	72.10	81.00	91.00				
3.75	54.90	60.30	66.40	73.60	82.10	91.80				
4.00	56.80	62.20	68.20	75.10	83.30	92.70				
4.25	58.80	64.20	70.00	76.70	84.60	93.70				
4.50	60.80	66.20	71.90	78.50	86.10	94.80				
4.75	62.80	68.20	73.90	80.30	87.60	96.10				
5.00	64.90	70.20	75.90	82.10	89.20	97.40				
5.25	67.00	72.30	77.90	84.00	90.90	98.80				

Dale Bud
10-18-07

5.50 69.10 74.40 79.90 85.90 92.70 . . . J

(Continued)

ACCEPTANCE LIMITS FOR DISSOLUTION (Q = 40.0)
 SAMPLING PLAN 2
 LOWER BOUND = 50.0, CONFIDENCE LEVEL = 99.0
 TABLE ENTRIES ARE LOWER LIMITS ON THE MEAN
 OF 6 ASSAYS- 2 ASSAYS AT EACH OF 3 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		
SE											
5.75	71.20	76.50	82.00	87.90	94.50						
6.00	73.30	78.60	84.00	89.90	96.30						
6.25	75.40	80.70	86.10	91.90	98.20						
6.50	77.50	82.80	88.20	93.80	99.90						
6.75	79.30	84.60	90.00	95.60							
7.00	81.10	86.40	91.70	97.30							
7.25	82.90	88.20	93.50	99.10							
7.50	84.70	90.00	95.30								
7.75	86.50	91.80	97.10								

Date 3/28
 10-18-07

8.00	88.40	93.60	98.90
8.25	90.20	95.40

(Continued)

ACCEPTANCE LIMITS FOR DISSOLUTION (Q = 40.0)
 SAMPLING PLAN 2
 LOWER BOUND = 50.0, CONFIDENCE LEVEL = 99.0
 TABLE ENTRIES ARE LOWER LIMITS ON THE MEAN
 OF 6 ASSAYS- 2 ASSAYS AT EACH OF 3 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
8.50	92.00	97.20
8.75	93.80	99.10
9.00	95.60
9.25	97.40
9.50	99.20

Doyle
10-18-07

FORM 6
PROBLEM/REQUEST REPORT

Name: Myron Diener

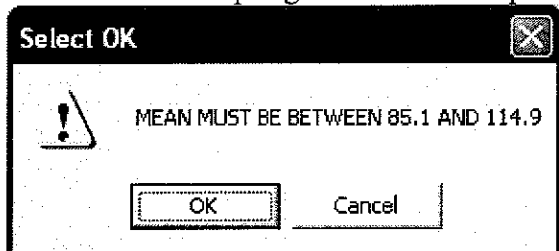
Date: 6/5/07

Describe the error or discrepancy in expected result verses found result or in expected performance of the program.

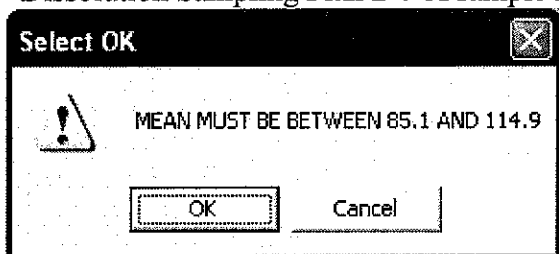
see attached

Supplement to Form 6: Observations in Navigation & Error Checks segment of the protocol (Appendix D), where the observed result deviated from the expected result.

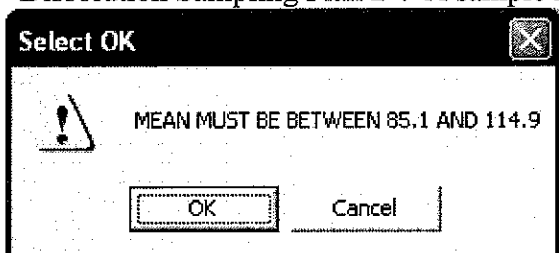
1. Error Screen observed in “Lower Bound Based on Sample Result” segment of “Dissolution Sampling Plan 1”. A sample mean of 75.1 was entered when $Q = 75$.



- 2.. Error Screen observed in “Lower Bound Based on Sample Result” segment of “Dissolution Sampling Plan 2”. A sample mean of 70.1 was entered when $Q = 60$.



- 3.. Error Screen observed in “Lower Bound Based on Sample Result” segment of “Dissolution Sampling Plan 2”. A sample mean of 80.6 was entered when $Q = 60$.



FORM 6
PROBLEM/REQUEST REPORT

Name: Myron Diener MD
Date: 6/13/07

Describe the error or discrepancy in expected result verses found result or in expected performance of the program.

Error screen expected and none observed as indicated in the protocol.

see attached

Supplement to Form 6: Observations in Navigation & Error Checks segment of the protocol (Appendix D), where the observed result deviated from the expected result.

1. Error Screen observed in "Lower Bound Based for a Specific Sample Result" segment of "Dissolution Sampling Plan 1". A sample mean of 75 was entered when $Q = 75$. The protocol stated that the expected response for this scenario is an error screen (ES). None was observed. The result from these parameters with all other parameters at the default settings is below.

**ACCEPTANCE LIMITS FOR DISSOLUTION (N = 6, Q = 75.0)
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
75	3	4	.000000113

2.. Error Screen observed in "Lower Bound Based for a Specific Sample Result" segment of "Dissolution Sampling Plan 2". A sample mean of 60 was entered when $Q = 60$. The protocol stated that the expected response for this scenario is an error screen (ES). None was observed. The result from these parameters with all other parameters at the default settings is below.

**ACCEPTANCE LIMITS FOR DISSOLUTION (Q = 60.0)
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
60	2.2	2.46	.002356815

FORM 6
PROBLEM/REQUEST REPORT

Name: James Pazdan

Date: 05/25/07

Describe the error or discrepancy in expected result verses found result or in expected performance of the program.

No logo appears on opening screen. See Attached.

NO LOGO



CONTENT UNIFORMITY AND DISSOLUTION ACCEPTANCE LIMITS

WRITTEN BY JAMES BERGUM

VERSION 2, REVISION 0

ENTER THE APPLICATION

EXIT SAS

SAS LOG:

```
1 ***** LIBRARY FOR THE APPLICATION*****;
```

```
2 /* deleting the macro variables */
```

```
3 data vars;
```

```
4 set sashelp.vmacro;
```

```
5 run;
```

NOTE: There were 45 observations read from the data set SASHELP.VMACRO.

NOTE: The data set WORK.VARS has 45 observations and 4 variables.

NOTE: DATA statement used:

real time	0.01 seconds
cpu time	0.01 seconds

```
6 data _null_;
```

```
7 set vars;
```

```
8 if scope='GLOBAL' and name ^= 'SYSODSPATH' then
```

```
9 call execute('%syndel '||trim(left(name))||'');
```

```
10 run;
```

NOTE: There were 45 observations read from the data set WORK.VARS.

NOTE: DATA statement used:

real time	0.01 seconds
cpu time	0.01 seconds

```
11
```

```
12 libname cudal 'H:\data\sasjimp\V2';
```

NOTE: Libref CUDAL was successfully assigned as follows:

Engine: V8

Physical Name: H:\DATA\SASJIMP\V2

```
13 options symbolgen mprint mlogic sasautos=('H:\data\sasjimp\V2');
```

```
14
```

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

WARNING: Cannot read external file C:\work\Jim\Version2\cudal.jpeg...

X error SAS/05

FORM 6
PROBLEM/REQUEST REPORT

Name: James Pazdan

Date: 08/17/07

Describe the error or discrepancy in expected result verses found result or in expected performance of the program.

See Attached.

Subject: Wrong Definition in Appendix E for Content Uniformity test

From: james.pazdan@novartis.com

Date: Fri, 17 Aug 2007 17:32:54 -0400

To: James S Bergum <james.bergum@bms.com>

Jim,

So after I got the "official" word from Jeff, it appears that the derivation in Appendix E for the lower bound used a simple distance of 25 for L2 from M, rather than 25% of M. It seems that way in the derivation for P(C22) as well.

Attached is my SAS program to do the simulations, with everything correct now, it now coincides with the SAS program you gave me (modified many times!) from Dennis.

The difference between using a 25% fraction of M vs. a distance of 25 from M (m has to be between 98.5 and 101.5) is trivial and less than 0.1% . Here are my simulations again:

Mean	Stdev	H=.001	H=.05 (Default)	Pass Test 1 Million Simulations	Pass S1	Pass S2 (Always Do S2 Bypass S1)	Pass S1 But Fail S2
100	7.39025	50.001	50.001	59.30	24.97	54.24	5.06
100	6.108	95.001	95.014	96.04	54.63	95.36	0.68
100	5.94782	97	97.0135	97.61	59.15	97.20	0.41
100	5.6605	99	99.013	99.24	67.67	99.11	0.14
95	5.7651	50.001	50.001	59.27	30.42	52.04	7.24
95	4.5697	95	94.9997	96.07	62.11	95.11	0.96
95	4.4322	97	96.9996	97.67	66.55	97.07	0.59
95	4.1919	99	98.9998	99.23	74.29	99.02	0.20
90	3.28388	50	50	57.47	29.66	50.01	7.46
90	2.58542	95.001	94.9984	95.97	61.99	94.98	0.98
90	2.50728	97	96.9984	97.59	66.48	96.97	0.62
90	2.371	99	98.9992	99.21	74.18	99.01	0.20

I added Pass S1 Bt Fails S2, as this is a major component of why the lower bound is conservative, it is better as a lower bound to just passing S2 (without doing S1 first.). It's conservative nature **doesn't** get less so much with mean away from 100, as with mean=90, S=3.28388, the lower bound is 50.0, while the simulated value is 57.5, but 50.01 passes S2 directly, 7.5% passes S1 and fails S2.

So what do you want to do about the wrong definition of the L2 criteria in S2? It makes so little difference and your bound is clearly conservative through out anyway from the simulated values.

Jim

sim_u du.sas Content-Type: application/octet-stream

FORM 6
PROBLEM/REQUEST REPORT

Name: _____David LeBlond_____

Date: _____September 26, 2007_____

Describe the error or discrepancy in expected result verses found result or in expected performance of the program.

See Attached. Independent Result does not match CuDAL program result.

Target	CI Level	Lower Bound	# Location	#/Location	SE	SM	CUDAL's Mean		SPLUS Code's Mean		Agree? (Y/N)
							Lower Bound	Upper Bound	Lower Bound	Upper Bound	
100.0	99.0	99.0	3	2	0.1	0.1	89.7	110.3	89.7	110.3	Y
					0.1	3.0	NA	NA	NA	NA	Y
					3.0	0.1	NA	NA	NA	NA	Y
					3.0	3.0	NA	NA	NA	NA	Y
				300	0.1	0.1	89.7	110.3	89.7	110.3	Y
					0.1	3.0	NA	NA	NA	NA	Y
					3.0	0.1	95.0	105.0	95.0	105.0	Y
					3.0	3.0	NA	NA	NA	NA	Y
			300	2	0.1	0.1	84.8	115.2	84.8	115.2	Y
					0.1	3.0	93.3	106.7	93.3	106.7	Y
					3.0	0.1	90.1	109.9	90.1	109.9	Y
					3.0	3.0	95.1	104.9	95.1	104.9	Y
				300	0.1	0.1	84.8	115.2	84.8	115.2	Y
					0.1	3.0	93.3	106.7	93.3	106.7	Y
					3.0	0.1	91.8	108.2	91.8	108.2	Y
					3.0	3.0	96.4	103.6	96.4	103.6	Y
102.5	50.0	50.0	3	2	0.1	3.0	96.8	103.2	96.8	104.2	N
	99.0	50.0	300	300	3.0	3.0	93.0	107.0	93.0	108.0	N
	99.0	50.0	3	2	0.1	0.1	88.6	111.4	88.6	112.4	N
				300	0.1	3.0	NA	NA	NA	NA	Y

Note: highlighted test cases not included in the protocol.

Support Documentation

INDEPENDENT RESULTS

1. Content Uniformity - Sampling Plan 1 / Splus Code

Exhibit 1.2: Splus Code to Compute Probability of Passing USP Test (“CUSP1.c1calc” related functions)

```
"CUSP1.c1calc"<-  
function(SIGMA,LLU,ULU,Target)  
{  
  n1<-10  
  k1<-2.4  
  L1<-15  
  n2<-30  
  k2<-2.0  
  L2<-24.625  
  h<-0.05  
  LM<-98.5  
  UM<-ifelse(Target <= 101.5,101.5,Target)  
  Overlbd<-CUSP1.c1calc.prob.c2(LLU,SIGMA,n1,k1,L1,n2,k2,L2,LM,UM,h)  
  Overubd<-CUSP1.c1calc.prob.c2(ULU,SIGMA,n1,k1,L1,n2,k2,L2,LM,UM,h)  
  min(Overlbd,Overubd)  
}  
  
"CUSP1.c1calc.prob.c1"<-  
function(U,SIGMA,n,k,L,LM,UM,h)  
{  
  I1<-(pnorm((UM-U)*sqrt(n)/SIGMA,0,1)-pnorm((LM-  
U)*sqrt(n)/SIGMA,0,1))*pchisq((n-1)*(L^2)/((k*SIGMA)^2),n-1)  
  a <- UM  
  b <- UM+L-h  
  I2<-(pnorm((c(seq(a,b,h))+h-U)*sqrt(n)/SIGMA,0,1)-pnorm((c(seq(a,b,h))-  
U)*sqrt(n)/SIGMA,0,1))*pchisq((n-1)*((UM+L-c(seq(a,b,h))-  
h/2)^2)/((k*SIGMA)^2),n-1)  
  I2<-sum(I2)  
  a <- LM-L  
  b <- LM-h  
  I3<-(pnorm((c(seq(a,b,h))+h-U)*sqrt(n)/SIGMA,0,1)-pnorm((c(seq(a,b,h))-  
U)*sqrt(n)/SIGMA,0,1))*pchisq((n-1)*((L-  
LM+c(seq(a,b,h))+h/2)^2)/((k*SIGMA)^2),n-1)  
  I3<-sum(I3)  
  I1+I2+I3  
}  
  
"CUSP1.c1calc.prob.c2"<-  
function(U,SIGMA,n1,k1,L1,n2,k2,L2,LM,UM,h)  
{  
  P1<-CUSP1.c1calc.prob.c1(U,SIGMA,n1,k1,L1,LM,UM,h)  
  C21<-CUSP1.c1calc.prob.c1(U,SIGMA,n2,k2,L1,LM,UM,h)  
  C22<-(pnorm((LM+L2-U)/SIGMA,0,1)-pnorm((UM-L2-U)/SIGMA,0,1))^n2  
  P2<-max(C21+C22-1,0)  
  max(P1,P2)  
}
```


Exhibit 1.2: Splus Code for “CUSP1.CALCUSP1” function for a specific mean

```
"CUSP1.CALCUSP1"<-
function(Target,CILEVEL,LBOUND,NUMBER,MEAN,Decimals)
{
  N<-NUMBER
  Z<- qnorm((1+sqrt(CILEVEL/100))/2,0,1)
  CHI <-qchisq(1-sqrt(CILEVEL/100),N-1)
  SAMPSD<-0.01
  while (SAMPSD <=7.8)
  {
    SIGMA<- sqrt((N - 1) * SAMPSD * SAMPSD / CHI)
    LLU<- MEAN - Z *SIGMA / sqrt(N)
    ULU<- MEAN + Z * SIGMA / sqrt(N)
    OVERBD<-CUSP1.clcalc(SIGMA,LLU,ULU,Target)
    if (OVERBD<(LBOUND/100))
    {
      if (SAMPSD>0.0101)
      {
        SAMPSD<-SAMPSD-0.001
        CV<-(100 * SAMPSD / MEAN)
        SAMPSD<-20.0
      }
      else
      {
        CV<-0
        SAMPSD<-20.0
      }
    }
    else
    {SAMPSD<-SAMPSD+0.001}
  }
  SAMPSD<- (CV*MEAN/100)
  CV<-floor((CV*(10^Decimals))+0.5)/(10^Decimals)
}
```

Exhibit 1.3: Test Output for Content Uniformity - Sampling Plan 1
(Using S-PLUS® 7.0 for Windows)

```
>
#####
> # Test Cases for CUSP1 (09-06-07)
> # Notes:
> # "OVERBD"-> Prob of passing test just after convergence
> # "SAMPSD"-> Sample S at the point of convergence
> # "CV"-> Coefficient of Variation (RSD) at the point of convergence
>
#####
> CUSP1.CALCUSP1(100, 50, 50, 5, 85.1, 2)
[1] 0.56
> OVERBD
[1] 0.4973655
> SAMPSD
[1] 0.479
> CV
[1] 0.56
> CUSP1.CALCUSP1(100, 50, 50, 5, 100, 2)
[1] 4.87
> OVERBD
[1] 0.499526
> SAMPSD
[1] 4.875
> CV
[1] 4.87
> CUSP1.CALCUSP1(100, 50, 50, 5, 114.9, 2)
[1] 0.42
> OVERBD
[1] 0.4973655
> SAMPSD
[1] 0.479
> CV
[1] 0.42
> #####
> CUSP1.CALCUSP1(100, 50, 50, 2000, 85.1, 2)
[1] 0.93
> OVERBD
[1] 0.496918
> SAMPSD
[1] 0.792
> CV
[1] 0.93
> CUSP1.CALCUSP1(100, 50, 50, 2000, 100, 2)
[1] 7.31
> OVERBD
[1] 0.4995609
> SAMPSD
[1] 7.307
> CV
[1] 7.31
> CUSP1.CALCUSP1(100, 50, 50, 2000, 114.9, 2)
[1] 0.69
> OVERBD
[1] 0.496918
> SAMPSD
[1] 0.792
> CV
[1] 0.69
> #####
> CUSP1.CALCUSP1(100, 99, 50, 5, 85.1, 2)
[1] 0.13
> OVERBD
[1] 0.4864842
> SAMPSD
[1] 0.112
> CV
[1] 0.13
> CUSP1.CALCUSP1(100, 99, 50, 5, 100, 2)
```

```

[1] 1.16
> OVERBD
[1] 0.4970256
> SAMPSD
[1] 1.157
> CV
[1] 1.16
> CUSP1.CALCUSP1(100, 99, 50, 5, 114.9, 2)
[1] 0.1
> OVERBD
[1] 0.4864842
> SAMPSD
[1] 0.112
> CV
[1] 0.1
> #####
> CUSP1.CALCUSP1(100, 99, 50, 2000, 85.1, 2)
[1] 0.88
> OVERBD
[1] 0.4995043
> SAMPSD
[1] 0.751
> CV
[1] 0.88
> CUSP1.CALCUSP1(100, 99, 50, 2000, 100, 2)
[1] 7.06
> OVERBD
[1] 0.4997461
> SAMPSD
[1] 7.059
> CV
[1] 7.06
> CUSP1.CALCUSP1(100, 99, 50, 2000, 114.9, 2)
[1] 0.65
> OVERBD
[1] 0.4995043
> SAMPSD
[1] 0.751
> CV
[1] 0.65
> #####
> CUSP1.CALCUSP1(100, 99, 99, 5, 85.1, 2)
[1] 0.11
> OVERBD
[1] 0.9861512
> SAMPSD
[1] 0.091
> CV
[1] 0.11
> CUSP1.CALCUSP1(100, 99, 99, 5, 100, 2)
[1] 0.94
> OVERBD
[1] 0.9897228
> SAMPSD
[1] 0.939
> CV
[1] 0.94
> CUSP1.CALCUSP1(100, 99, 99, 5, 114.9, 2)
[1] 0.08
> OVERBD
[1] 0.9861512
> SAMPSD
[1] 0.091
> CV
[1] 0.08
> #####
> CUSP1.CALCUSP1(100, 99, 99, 2000, 85.1, 2)
[1] 0.64
> OVERBD
[1] 0.989988
> SAMPSD

```

```

[1] 0.546
> CV
[1] 0.64
> CUSP1.CALCUSP1(100, 99, 99, 2000, 100, 2)
[1] 5.41
> OVERBD
[1] 0.9899861
> SAMPSD
[1] 5.413
> CV
[1] 5.41
> CUSP1.CALCUSP1(100, 99, 99, 2000, 114.9, 2)
[1] 0.48
> OVERBD
[1] 0.989988
> SAMPSD
[1] 0.546
> CV
[1] 0.48
> #####
> CUSP1.CALCUSP1(104.5, 50, 50, 5, 85.1, 2)
[1] 0.56
> OVERBD
[1] 0.4973655
> SAMPSD
[1] 0.479
> CV
[1] 0.56
> CUSP1.CALCUSP1(104.5, 50, 50, 5, 100, 2)
[1] 4.75
> OVERBD
[1] 0.4995082
> SAMPSD
[1] 4.752
> CV
[1] 4.75
> CUSP1.CALCUSP1(104.5, 50, 50, 5, 114.9, 2)
[1] 1.2
> OVERBD
[1] 0.4982063
> SAMPSD
[1] 1.378
> CV
[1] 1.2
> #####
> CUSP1.CALCUSP1(104.5, 50, 50, 2000, 85.1, 2)
[1] 0.93
> OVERBD
[1] 0.496918
> SAMPSD
[1] 0.792
> CV
[1] 0.93
> CUSP1.CALCUSP1(104.5, 50, 50, 2000, 100, 2)
[1] 7.21
> OVERBD
[1] 0.4995294
> SAMPSD
[1] 7.207
> CV
[1] 7.21
> CUSP1.CALCUSP1(104.5, 50, 50, 2000, 114.9, 2)
[1] 1.98
> OVERBD
[1] 0.499009
> SAMPSD
[1] 2.272
> CV
[1] 1.98
> #####
> CUSP1.CALCUSP1(104.5, 99, 50, 5, 85.1, 2)

```

```

[1] 0.13
> OVERBD
[1] 0.4864842
> SAMPSD
[1] 0.112
> CV
[1] 0.13
> CUSP1.CALCUSP1(104.5, 99, 50, 5, 100, 2)
[1] 1.14
> OVERBD
[1] 0.497357
> SAMPSD
[1] 1.138
> CV
[1] 1.14
> CUSP1.CALCUSP1(104.5, 99, 50, 5, 114.9, 2)
[1] 0.28
> OVERBD
[1] 0.4972583
> SAMPSD
[1] 0.323
> CV
[1] 0.28
> #####
> CUSP1.CALCUSP1(104.5, 99, 50, 2000, 85.1, 2)
[1] 0.88
> OVERBD
[1] 0.4995043
> SAMPSD
[1] 0.751
> CV
[1] 0.88
> CUSP1.CALCUSP1(104.5, 99, 50, 2000, 100, 2)
[1] 6.94
> OVERBD
[1] 0.4998806
> SAMPSD
[1] 6.942
> CV
[1] 6.94
> CUSP1.CALCUSP1(104.5, 99, 50, 2000, 114.9, 2)
[1] 1.88
> OVERBD
[1] 0.4993709
> SAMPSD
[1] 2.157
> CV
[1] 1.88
> #####
> CUSP1.CALCUSP1(104.5, 99, 99, 5, 85.1, 2)
[1] 0.11
> OVERBD
[1] 0.9861512
> SAMPSD
[1] 0.091
> CV
[1] 0.11
> CUSP1.CALCUSP1(104.5, 99, 99, 5, 100, 2)
[1] 0.93
> OVERBD
[1] 0.9899098
> SAMPSD
[1] 0.927
> CV
[1] 0.93
> CUSP1.CALCUSP1(104.5, 99, 99, 5, 114.9, 2)
[1] 0.23
> OVERBD
[1] 0.989965
> SAMPSD
[1] 0.261

```

```
> CV
[1] 0.23
> #####
> CUSP1.CALCUSP1(104.5, 99, 99, 2000, 85.1, 2)
[1] 0.64
> OVERBD
[1] 0.989988
> SAMPSD
[1] 0.546
> CV
[1] 0.64
> CUSP1.CALCUSP1(104.5, 99, 99, 2000, 100, 2)
[1] 5.29
> OVERBD
[1] 0.9899766
> SAMPSD
[1] 5.293
> CV
[1] 5.29
> CUSP1.CALCUSP1(104.5, 99, 99, 2000, 114.9, 2)
[1] 1.37
> OVERBD
[1] 0.9899379
> SAMPSD
[1] 1.573
> CV
[1] 1.37
```

INDEPENDENT RESULTS

2. Content Uniformity - Sampling Plan 2 / Splus Code

Exhibit 2.1: Splus Code for Content Uniformity - Sampling Plan 2 (CUSP2)

```
"CUSP2.cullu"<-
function(MEAN,Z,MVAR,N,SIGMA,Target)
{
  LLU<-(MEAN-(Z*sqrt(MVAR/N)))
  UM<-ifelse(Target <= 101.5,101.5,Target)
  CUSP1.clcalc.prob.c2(LLU,SIGMA,10,2.4,15,30,2,24.625,98.5,UM,0.05)
}

"CUSP2.cuulu"<-
function(MEAN,Z,MVAR,N,SIGMA,Target)
{
  ULU<-(MEAN+(Z*sqrt(MVAR/N)))
  UM<-ifelse(Target <= 101.5,101.5,Target)
  CUSP1.clcalc.prob.c2(ULU,SIGMA,10,2.4,15,30,2,24.625,98.5,UM,0.05)
}

"CUSP2.CALCUSP2"<-
function(Target,CILEVEL,LBOUND,LOC,NUM,SE,SM,Decimals)
{
  D<-0.10
  SEBOUND<-9.2
  SMLIM<-9.2
  MEANL<-84.9
  MEANU<-115.1

  Z<-qnorm((1+sqrt(CILEVEL/100))/2,0,1)
  NN<-NUM
  L<-LOC
  N<-NN*L
  CHIERR<-qchisq(1-sqrt(CILEVEL/100),L*(NN-1))
  CHILOC<-qchisq(1-sqrt(CILEVEL/100),L-1)
  SMBOUND<-SMLIM
  SE2<-SE*SE
  H2<-(L*(NN-1)/CHIERR-1)
  SEC<-(((1-1/NN)*H2*SE2)^2)
  if (is.na(MEANL)==F)
  {
    SL2<-(SM*SM*NN)
    SL2UB<-((L-1)*SL2/CHILOC)
    H1<-((L-1)/CHILOC-1)
    FIRST<-(((1/NN)*H1*SL2)^2)
    PTEST<-((1/NN)*SL2+(1-1/NN)*SE2)
    VAR<-(PTEST+sqrt(FIRST+SEC))
    MVAR<-SL2UB
    SIGMA<-sqrt(VAR)
    MEAN<-(MEANL-D)
    OUT<-0
    while (MEAN<=115.5)
    {
      OVERBDL<-CUSP2.cullu(MEAN,Z,MVAR,N,SIGMA,Target)
      if (OVERBDL>(LBOUND/100))
      {
        MEANL<-MEAN
        OUT<-1
        MEAN<-115.6
      }
    }
  }
}
```

```

        MEAN<-(MEAN+D)
    }
    if (OUT==1) {MEAN<-MEANL}
    if (OVERBDL<=(LBOUND/100))
    {
        MEANL<-NA
        MEANU<-NA
        if (SE==D)
        {
            SMLIM<-(SM-D)
            SM<-10
        }
        else {if (SM==D){SE<-10}}
    }
    else
    {
        MEAN<-(MEANU+D)
        OUT<-0
        while (MEAN>=84.9)
        {
            OVERBDU<-CUSP2.cuulu(MEAN,Z,MVAR,N,SIGMA,Target)
            if (OVERBDU >(LBOUND/100))
            {
                MEANU<-MEAN
                OUT<-1
                MEAN<-84.8
            }
            else
            {MEAN<-(MEAN-D)}
        }
        if (OUT==1) {MEAN<-MEANU}
        if ((MEANU<=MEANL) || (MEAN<=MEANL))
        {
            MEANL<-NA
            MEANU<-NA
        }
    }
    MEANL<-floor((MEANL*(10^Decimals))+0.5)/(10^Decimals)
    MEANU<-floor((MEANU*(10^Decimals))+0.5)/(10^Decimals)
}

```


Exhibit 1.2: Splus Code from CUSP1 used by CUSP2

```
"CUSP1.clcalc.prob.c1"<-
function(U,SIGMA,n,k,L,LM,UM,h)
{
  I1<-(pnorm((UM-U)*sqrt(n)/SIGMA,0,1)-pnorm((LM-
U)*sqrt(n)/SIGMA,0,1))*pchisq((n-1)*(L^2)/((k*SIGMA)^2),n-1)
  a <- UM
  b <- UM+L-h
  I2<-(pnorm((c(seq(a,b,h))+h-U)*sqrt(n)/SIGMA,0,1)-pnorm((c(seq(a,b,h))-
U)*sqrt(n)/SIGMA,0,1))*pchisq((n-1)*((UM+L-c(seq(a,b,h))-
h/2)^2)/((k*SIGMA)^2),n-1)
  I2<-sum(I2)
  a <- LM-L
  b <- LM-h
  I3<-(pnorm((c(seq(a,b,h))+h-U)*sqrt(n)/SIGMA,0,1)-pnorm((c(seq(a,b,h))-
U)*sqrt(n)/SIGMA,0,1))*pchisq((n-1)*((L-
LM+c(seq(a,b,h))+h/2)^2)/((k*SIGMA)^2),n-1)
  I3<-sum(I3)
  I1+I2+I3
}

"CUSP1.clcalc.prob.c2"<-
function(U,SIGMA,n1,k1,L1,n2,k2,L2,LM,UM,h)
{
  P1<-CUSP1.clcalc.prob.c1(U,SIGMA,n1,k1,L1,LM,UM,h)
  C21<-CUSP1.clcalc.prob.c1(U,SIGMA,n2,k2,L1,LM,UM,h)
  C22<-(pnorm((LM+L2-U)/SIGMA,0,1)-pnorm((UM-L2-U)/SIGMA,0,1))^n2
  P2<-max(C21+C22-1,0)
  max(P1,P2)
}
```

Exhibit 1.3: Test Output for CUSP2 (Using S-PLUS® 7.0 for Windows)

```
> #####
> # Test Cases for CUSP2 (09-07-07)
> # Notes:
> # "MEANL"-> Lower bound for Mean
> # "MEANU"-> Upper bound for Mean
> #####
> CUSP2.CALCUSP2(100, 50, 50, 3, 2, 0.1, 0.1, 1)
[1] 115.2
> MEANL
[1] 84.8
> MEANU
[1] 115.2
> CUSP2.CALCUSP2(100, 50, 50, 3, 2, 0.1, 3, 1)
[1] 103.2
> MEANL
[1] 96.8
> MEANU
[1] 103.2
> CUSP2.CALCUSP2(100, 50, 50, 3, 2, 3, 0.1, 1)
[1] 110.2
> MEANL
[1] 89.8
> MEANU
[1] 110.2
> CUSP2.CALCUSP2(100, 50, 50, 3, 2, 3, 3, 1)
[1] 102.2
> MEANL
[1] 97.8
> MEANU
[1] 102.2
```

```

> #####
> CUSP2.CALCUSP2(100, 50, 50, 3, 300, 0.1, 0.1, 1)
[1] 115.2
> MEANL
[1] 84.8
> MEANU
[1] 115.2
> CUSP2.CALCUSP2(100, 50, 50, 3, 300, 0.1, 3, 1)
[1] 103.2
> MEANL
[1] 96.8
> MEANU
[1] 103.2
> CUSP2.CALCUSP2(100, 50, 50, 3, 300, 3, 0.1, 1)
[1] 110.3
> MEANL
[1] 89.7
> MEANU
[1] 110.3
> CUSP2.CALCUSP2(100, 50, 50, 3, 300, 3, 3, 1)
[1] 101.5
> MEANL
[1] 98.5
> MEANU
[1] 101.5
> #####
> CUSP2.CALCUSP2(100, 50, 50, 300, 2, 0.1, 0.1, 1)
[1] 115.2
> MEANL
[1] 84.8
> MEANU
[1] 115.2
> CUSP2.CALCUSP2(100, 50, 50, 300, 2, 0.1, 3, 1)
[1] 110.2
> MEANL
[1] 89.8
> MEANU
[1] 110.2
> CUSP2.CALCUSP2(100, 50, 50, 300, 2, 3, 0.1, 1)
[1] 112.1
> MEANL
[1] 87.9
> MEANU
[1] 112.1
> CUSP2.CALCUSP2(100, 50, 50, 300, 2, 3, 3, 1)
[1] 108.9
> MEANL
[1] 91.1
> MEANU
[1] 108.9
> #####
> CUSP2.CALCUSP2(100, 50, 50, 300, 300, 0.1, 0.1, 1)
[1] 115.2
> MEANL
[1] 84.8
> MEANU
[1] 115.2
> CUSP2.CALCUSP2(100, 50, 50, 300, 300, 0.1, 3, 1)
[1] 110.2
> MEANL
[1] 89.8
> MEANU
[1] 110.2
> CUSP2.CALCUSP2(100, 50, 50, 300, 300, 3, 0.1, 1)
[1] 110.5
> MEANL
[1] 89.5

```

```

> MEANU
[1] 110.5
> CUSP2.CALCUSP2(100, 50, 50, 300, 300, 3, 3, 1)
[1] 107.8
> MEANL
[1] 92.2
> MEANU
[1] 107.8
> #####
> CUSP2.CALCUSP2(100, 50, 99, 3, 2, 0.1, 0.1, 1)
[1] 115.2
> MEANL
[1] 84.8
> MEANU
[1] 115.2
> CUSP2.CALCUSP2(100, 50, 99, 3, 2, 0.1, 3, 1)
[1] NA
> MEANL
[1] NA
> MEANU
[1] NA
> CUSP2.CALCUSP2(100, 50, 99, 3, 2, 3, 0.1, 1)
[1] 107.8
> MEANL
[1] 92.2
> MEANU
[1] 107.8
> CUSP2.CALCUSP2(100, 50, 99, 3, 2, 3, 3, 1)
[1] NA
> MEANL
[1] NA
> MEANU
[1] NA
> #####
> CUSP2.CALCUSP2(100, 50, 99, 3, 300, 0.1, 0.1, 1)
[1] 115.2
> MEANL
[1] 84.8
> MEANU
[1] 115.2
> CUSP2.CALCUSP2(100, 50, 99, 3, 300, 0.1, 3, 1)
[1] NA
> MEANL
[1] NA
> MEANU
[1] NA
> CUSP2.CALCUSP2(100, 50, 99, 3, 300, 3, 0.1, 1)
[1] 108
> MEANL
[1] 92
> MEANU
[1] 108
> CUSP2.CALCUSP2(100, 50, 99, 3, 300, 3, 3, 1)
[1] NA
> MEANL
[1] NA
> MEANU
[1] NA
> #####
> CUSP2.CALCUSP2(100, 50, 99, 300, 2, 0.1, 0.1, 1)
[1] 115.2
> MEANL
[1] 84.8
> MEANU
[1] 115.2
> CUSP2.CALCUSP2(100, 50, 99, 300, 2, 0.1, 3, 1)
[1] 107.8

```

```

> MEANL
[1] 92.2
> MEANU
[1] 107.8
> CUSP2.CALCUSP2(100, 50, 99, 300, 2, 3, 0.1, 1)
[1] 110.5
> MEANL
[1] 89.5
> MEANU
[1] 110.5
> CUSP2.CALCUSP2(100, 50, 99, 300, 2, 3, 3, 1)
[1] 106
> MEANL
[1] 94
> MEANU
[1] 106
> #####
> CUSP2.CALCUSP2(100, 50, 99, 300, 300, 0.1, 0.1, 1)
[1] 115.2
> MEANL
[1] 84.8
> MEANU
[1] 115.2
> CUSP2.CALCUSP2(100, 50, 99, 300, 300, 0.1, 3, 1)
[1] 107.8
> MEANL
[1] 92.2
> MEANU
[1] 107.8
> CUSP2.CALCUSP2(100, 50, 99, 300, 300, 3, 0.1, 1)
[1] 108.2
> MEANL
[1] 91.8
> MEANU
[1] 108.2
> CUSP2.CALCUSP2(100, 50, 99, 300, 300, 3, 3, 1)
[1] 104.5
> MEANL
[1] 95.5
> MEANU
[1] 104.5
> #####
> CUSP2.CALCUSP2(100, 99, 99, 3, 2, 0.1, 0.1, 1)
[1] 110.3
> MEANL
[1] 89.7
> MEANU
[1] 110.3
> CUSP2.CALCUSP2(100, 99, 99, 3, 2, 0.1, 3, 1)
[1] NA
> MEANL
[1] NA
> MEANU
[1] NA
> CUSP2.CALCUSP2(100, 99, 99, 3, 2, 3, 0.1, 1)
[1] NA
> MEANL
[1] NA
> MEANU
[1] NA
> CUSP2.CALCUSP2(100, 99, 99, 3, 2, 3, 3, 1)
[1] NA
> MEANL
[1] NA
> MEANU
[1] NA
> #####

```

```

> CUSP2.CALCUSP2(100, 99, 99, 3, 300, 0.1, 0.1, 1)
[1] 110.3
> MEANL
[1] 89.7
> MEANU
[1] 110.3
> CUSP2.CALCUSP2(100, 99, 99, 3, 300, 0.1, 3, 1)
[1] NA
> MEANL
[1] NA
> MEANU
[1] NA
> CUSP2.CALCUSP2(100, 99, 99, 3, 300, 3, 0.1, 1)
[1] 105
> MEANL
[1] 95
> MEANU
[1] 105
> CUSP2.CALCUSP2(100, 99, 99, 3, 300, 3, 3, 1)
[1] NA
> MEANL
[1] NA
> MEANU
[1] NA
> #####
> CUSP2.CALCUSP2(100, 99, 99, 300, 2, 0.1, 0.1, 1)
[1] 115.2
> MEANL
[1] 84.8
> MEANU
[1] 115.2
> CUSP2.CALCUSP2(100, 99, 99, 300, 2, 0.1, 3, 1)
[1] 106.7
> MEANL
[1] 93.3
> MEANU
[1] 106.7
> CUSP2.CALCUSP2(100, 99, 99, 300, 2, 3, 0.1, 1)
[1] 109.9
> MEANL
[1] 90.1
> MEANU
[1] 109.9
> CUSP2.CALCUSP2(100, 99, 99, 300, 2, 3, 3, 1)
[1] 104.9
> MEANL
[1] 95.1
> MEANU
[1] 104.9
> #####
> CUSP2.CALCUSP2(100, 99, 99, 300, 300, 0.1, 0.1, 1)
[1] 115.2
> MEANL
[1] 84.8
> MEANU
[1] 115.2
> CUSP2.CALCUSP2(100, 99, 99, 300, 300, 0.1, 3, 1)
[1] 106.7
> MEANL
[1] 93.3
> MEANU
[1] 106.7
> CUSP2.CALCUSP2(100, 99, 99, 300, 300, 3, 0.1, 1)
[1] 108.2
> MEANL
[1] 91.8
> MEANU

```

```

[1] 108.2
> CUSP2.CALCUSP2(100, 99, 99, 300, 300, 3, 3, 1)
[1] 103.6
> MEANL
[1] 96.4
> MEANU
[1] 103.6
> #####
> CUSP2.CALCUSP2(102.5, 50, 50, 3, 2, 0.1, 3, 1)
[1] 104.2
> MEANL
[1] 96.8
> MEANU
[1] 104.2
> CUSP2.CALCUSP2(102.5, 99, 50, 300, 300, 3, 3, 1)
[1] 108
> MEANL
[1] 93
> MEANU
[1] 108
> CUSP2.CALCUSP2(102.5, 99, 50, 3, 2, 0.1, 0.1, 1)
[1] 112.4
> MEANL
[1] 88.6
> MEANU
[1] 112.4
> CUSP2.CALCUSP2(102.5, 99, 50, 3, 300, 0.1, 3, 1)
[1] NA
> MEANL
[1] NA
> MEANU
[1] NA

```

VITA'S*

* Includes Plinio De Los Santos, Jr.'s vita. Plinio wrote the SPLUS program to provide an independent calculation of the CuDAL acceptance limits.

CURRICULUM VITAE

Name: **Merlin L Utter**
16 Cottage Place
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Date: October 19, 2007
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EMPLOYMENT

1984 - Present Wyeth Pharmaceuticals

Manager, Statistical Services, Quality Assurance, Wyeth Pharmaceuticals Oct 2000 - Present
Supervised group of up to 3 full time statisticians and 2 part-time consultants performing functions discussed below. Duties include monitoring the progress of projects, helping to direct the group's activities to meet organizational priorities, reviewing the technical content and business relevance of the department reports, etc.

Statistical Consultant, Quality Assurance, Wyeth Pharmaceuticals 1994 – Oct. 2000
Provided statistical support to the Quality Assurance, and Manufacturing functions of Wyeth Pharmaceuticals. Activities included the design and analysis of validation data, the setting of release limits from stability data, statistical support for batch release and product contamination decisions, investigations of laboratory/manufacturing problems, response to regulatory issues, and support for the implementation of statistical process control within the plant.

Statistical Consultant, Quality Management, Std Prods Factory, Lederle 1994
Provided statistical support similar to the above but to the Quality Assurance, and Manufacturing functions within the Standard Products focused factory of Lederle Laboratories.

Statistical Consultant, Quality Management, Lederle Laboratories 1984 - 1994
Provided statistical support similar to the above, but as part of a group that serviced the entire Lederle Division. Hired two statisticians and managed group for the last two years.

1974-1983 The Procter and Gamble Company

Biometrician, Beauty Care Division 1981 - 1983
Provided a leadership role in the design and execution of hair and skin clinical studies. Responsibilities included helping the project teams plan both their current and long-term clinical needs as well as design, analyze and interpret test results for all clinical studies. Managed three people in this role.

Statistical Consultant, Toilet Goods Division 1980 - 1981
Responsible for providing statistical consulting in the areas of Process and Product Development, Products Research, and Regulatory. Provided statistical support in such areas as claim substantiation, design and analysis of data for both laboratory and consumer testing, and design of experiments for process optimization.

Internal Corporate Consultant

1974 - 1980

Consulted with both on-site and remote locations in the areas of Manufacturing and Product Development, specializing in the solving of a wide assortment of quality control/quality assurance problems as well as cost savings opportunities. Also consulted in the areas of R&D, Engineering, General Advertising, Sales and Marketing.

EDUCATION

Rensselaer Polytechnic Institute; Troy, New York

1974 Ph. D. - Statistics and Operations Research
NSF Fellowship, GPA=4.0/4.0

Dissertation: Robustness of Experimental Designs and Various Optimality Criteria

1971 M. S. - Statistics and Operations Research
Full-time teaching assistant, NSF Research Summer Grant, GPA=3.8/4.0

1969 B. S. - Mathematics
Dean's List, Cum Laude, GPA=3.5/4.0

PUBLICATIONS

Statistical Process Control and Process Capability (with T. Murphy and S. Singh), Encyclopedia of Pharmaceutical Technology, Marcel Dekker (2003).

Statistical Methods for Uniformity and Dissolution Testing (with J. Bergum), Pharmaceutical Process Validation, 667-697, R. Nash and A. Wachter ed., Marcel Dekker (2003).

Process Validation, (with J. Bergum), Encyclopedia of Biopharmaceutical Statistics, 422-439, Shein-Chun Chow ed., Marcel Dekker (2000).

Co-author (with PhRMA Statistics Subteam) of four stimuli articles on ICH Proposed Dose Uniformity Test Requirements, Pharm Forum (1997, 1998, 1999, 1999), as well as numerous other PhRMA Statistics Expert Team Subteam publications.

"An Evaluation of the Pooled Dissolution Test Acceptance Sampling Procedure for Pooled Samples", (with R. Wojcik and A. Zimmermann), Pharm Forum, 1995 (21,4), 1169-1175

"Cyclical Job Sequencing on Multiple Sets of Identical Machines," (with H. Stern and E. Rodriguez), Naval Research Logistics Quarterly, 1977, 24 (1), 137-151.

PRESENTATIONS

Moderator for session (Design of Stability Studies to Set Specifications) at AAPS Workshop on Specifications for Biotechnology and Biological Products (2004)

Organizer/moderator/speaker for session on Process Validation, Muncie Statistical Meetings (1990)

PROFESSIONAL AFFILIATIONS

American Statistical Association

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OBJECTIVE:

A position involving the use of applied statistics and operations research techniques.

EDUCATION:

- ***Rensselaer Polytechnic Institute- Troy, N.Y.***
Ph.D., Decision Sciences & Engineering Systems
Completion date: 12/98. GPA: 3.92.
Doctoral Thesis: "Statistical Methods for Estimating and Characterizing Social Welfare Recipient Payments."
- ***Rensselaer Polytechnic Institute - Troy, N.Y.***
Master of Science in Industrial and Management Engineering
Applied Probability, Statistics and Quality Control concentration.
Completion date: 05/96. GPA: 3.90.
- ***University of Puerto Rico - Rio Piedras Campus, P.R.***
Master of Business Administration.
Completion date: 12/92. GPA: 3.87.
- ***Technological Institute of Santo Domingo - Dominican Republic***
Bachelor of Science in Industrial Engineering (Summa Cum Laude)
Completion date: 10/86. GPA: 3.84.

JOB EXPERIENCE:

- ***Wyeth Pharmaceuticals*** , Pearl River, NY (07/2001 to present)
Senior Statistician
Provides global statistical support to internal clients across Wyeth manufacturing operations. Statistical projects cover the following areas:
 - a) Analysis of stability data using fixed effects and mixed effects linear models to calculate internal specifications, to revise the expiry period or to revise the shelf specifications.
 - b) Analysis of environmental monitoring data using both parametric and nonparametric approaches to establish tolerance or percentile based alert and action limits.
 - c) Analysis of release data and stability to establish control limits and overages of nutritional products.
 - d) Analysis of in-process manufacturing data using SPC and process capability techniques.
 - e) Developed sampling plans to gather information for batch release and for software validation testing.
 - f) Development, validation, training and deployment of statistical applications to assist QA product support specialists in their evaluation of release and stability data and to assist personnel in raw material labs in reduced testing evaluations.
 - g) Development of simulation programs to determine probability of passing product tests (such as content uniformity and dissolution USP tests).
 - h) Development of programs for real time detection of atypical test results.
- ***MicroStrategy Inc.***, Vienna, VA (03/1999 to 07/2001)
Principal Software Quality Engineer
Performed simulation-based scalability testing and data analysis for e-business/OLAP application development projects. Estimated hardware requirements under clustered environments. These tasks required exposure to web-application stress tools (like WAST), multiple RDBMS (such as Oracle, SQL Server and MS Access) and machine clustering solutions (like Cisco's LocalDirector).
- ***Rensselaer Statistical Consulting Center***, Troy, N.Y. (01/1996 to 12/1998)
Research Assistant

Applied statistical methods in public administration and medical research projects. These projects required the development of techniques for multi-period sampling, nonparametric imputation of missing data and survival analysis of social welfare data. Additionally, some of these projects require the analysis of categorical data.

- **Schein Pharmaceutical Inc.**, Carmel N.Y. (Summer/1995)

Consultant

Performed re-organization analysis of drug stability department. Project required the use of integer programming for approaching resource allocation issues. Also, project required the evaluation of sampling and regression approaches employed in the analysis of drug-stability data.

- **Warner Lambert Inc.**, Fajardo, P.R. (05/1993 to 06/1994)

Pharmaceutical Technologist

Performed statistical data analysis of process and product validation projects using the following techniques: multiple regression analysis, design of experiments, SPC and acceptance sampling. Also performed project management of GMP compliance projects and product reformulation bio-studies.

CONTINUAL EDUCATION COURSES:

- SQL fundamentals (Boot Camp T3-99, MicroStrategy University, VA, 1999).
- ASP and XML courses (MicroStrategy University, VA, 2000).
- A Journey into Regulatory Compliance: An Introduction in 21 CFR Part 11.03 (JSM 2002, NYC)
- A Short-Course on Mixed Models and Covariance Structures (NJ Chapter of ASA, 04/2002)
- Analyzing Mixed Effect Models with S-Plus (Insightful Corporation, Philadelphia PA, 10/2003).
- Multivariate Data Analysis (Umetrics, Montreal-Canada, 11/2005)

MEMBERSHIPS: American Statistical Association (ASA) and IEEE Computer Society.

REFeree JOURNAL PUBLICATIONS:

- De los Santos, P., R.J. Burke and J.M. Tien, "Progressive Random Sampling: A Multi-Period Estimation Technique with Applications," *IEEE Transactions on Systems, Man and Cybernetics Part C: Applications and Reviews*, V.30 No.4 (November 2000), p.p.418-426.
- De los Santos, P., R.J. Burke and J.M. Tien, "Progressive Random Sampling with Stratification," *IEEE Transactions on Systems, Man and Cybernetics Part C: Applications and Reviews*. (Accepted for Publication on 03/2007).

ACADEMIC AWARDS:

- 1986 CODETEL Excellence Award, Technological Institute of Santo Domingo.
- 1993 Popular Bank First Century Award, Graduate Business School of University of Puerto Rico.
- 1994 Rensselaer Polytechnic Institute Topper Award.
- 1996 and 1998 General Electric Academic Awards.
- 1998 Rensselaer Polytechnic Institute Founders Award of Excellence.
- 2000 Del and Ruth Kager Dissertation Award.

COMPUTER SKILLS:

<i>Application Area</i>	<i>Programs</i>
Statistics	SAS, Splus, Minitab, JMP, Spotfire, Statgraphics
RDBMS (SQL)	MS Access, Oracle and SQL Server
Simulation modeling	Siman, Arena
Mathematical programming	Lingo, Ampl
General purpose programming	FORTRAN
Project management	MS Project, Time Line

Note: Also familiarity with Windows 95, 98, NT, 2000, XP and UNIX operating systems.

LANGUAGES: English and Spanish.

CITIZENSHIP STATUS: US Citizen.



Curriculum Vitae

A. Brent Harrington
2 Woodhull Drive
Campbell Hall, NY, 10916
USA

Phone: 845-602-3028
Fax: 845-602-3355
Email: Harrinb@wyeth.com

Current Job Responsibilities

Dates: July 2006 – Present
Company: Wyeth
Location: Pearl River, NY, USA
Title: Assistant Director

Job Responsibilities: Direct staff members providing statistical and programming support for the analysis of preclinical CP&D projects. Serve as the primary liaison with CP&D management. Responsible for applying high-level statistical expertise to preclinical formulation and analytical development processes. Develop statistical methodology applicable to the preclinical development process. Maintain familiarity with the relevant literature. Identify opportunities to utilize innovative statistical methodology to streamline the preclinical development process and facilitate optimal decision-making. Direct and guide staff members in choice of statistical methodology and study design to meet client's goals. Define, evaluate, and enforce department SOPs and guidelines to ensure adherence to company/departmental standards. Serve as statistical expert on CPD Specification Committee and Equine Advisory Board.

Professional Experience

Dates: Feb 1990 – June 1992 Statistical Associate
June 1992 – Nov 1995 Statistician
Nov 1995 – June 1998 Senior Statistician
June 1998 – June 2001 Principal Statistician
June 2001 – June 2006 Senior Principal Statistician
June 2006 – Present Assistant Director
Company/Institution: Wyeth
Location: Pearl River, NY, USA

Education

Institution: Virginia Tech
Location: Blacksburg, Virginia, USA
Degree: M.S. Statistics

Institution: Virginia Tech
Location: Blacksburg, Virginia, USA
Degree: B.S. Statistics/Minor Mathematics

Professional Memberships

Member American Statistical Association
Member American Association of Pharmaceutical Scientists

Patents/Publications

Formulation Development and Stability Determination
Chapter in upcoming book to be published in 2007

Use of Matrix Designs in Drug Stability Studies
Presentation at DIA Conference, October 2004

Determining Specifications on Multi-component Products
Paper presented at the Midwest Biopharmaceutical Statistics Workshop in
Muncie, Indiana, May 1994

Awards

Wyeth Team Awards – 2005 CPD Zosyn EF Development Team
Multiple Premarin Specifications Team Awards

RESUME (08/01/2007)

I. PERSONAL DATA

A. Name: ***Edith Tan Senderak***

B. Home Address: **2988 Horseshoe Drive
Collegeville, PA 19426**

C. Home Telephone: **(610) 584-9516**

II. EDUCATION

<u>School</u>	<u>Date</u>	<u>Major/Minor Courses</u>	<u>Degree</u>
Virginia Polytechnic Institute and State University	1981/1987	Statistics	M.S./ Ph.D.
University of the Philippines	1979	Statistics	B.S. (cum laude)

III. MERCK/MRL EMPLOYMENT HISTORY (most recent first)

<u>Title</u>	<u>From - To</u>
Associate Director, Nonclinical Statistics Responsible for the supervision of a Senior Biometrician and Biometrician providing statistical support to the departments of Pharmaceutical Research and Development and Global Pharmaceutical Commercialization. Provided statistical support to Bioprocess Research and Development. Responsible for developing and conducting workshops on DOE software packages.	2005 - 2007
Long-Term Disability Leave	2003 - 2005
Associate Director, Biometrics Research Responsible for the supervision, mentoring, and guidance of a Ph. D. Biometrician providing statistical support to the departments of Pharmaceutical Research and Development and Cancer Research. Conducted/led seminars and discussions on development and regulatory issues for PR&D. Provided designs and analyses for long-term stability studies, assay development, formulation, and process development in support of regulatory submissions. Responsible for addressing regulatory concerns or comments in CMC section of submission.	1999 - 2003
Senior Biometrician, Biometrics Research/Vaccine-Biometrics Research Responsible for providing statistical support to Pharmaceutical Research	1992 - 1999

and Development. Analyzed and prepared statistical reports on long-term stability studies for NDA submissions, and in support of submissions to regulatory agencies in other countries. Provided and evaluated matrix designs for use in long-term stability studies. Addressed regulatory agencies' comments on stability issues in CMC section of submission. Worked with colleagues from Pharmaceutical Research and Development in the design, analysis, and interpretation of results from formulation and process development experiments.

Statistical Consultant to the Departments of Cancer Research, Virus and Cell Biology, Vaccine - Human Serology, Biological Chemistry, Vaccine Analytical Research, Bioprocess R & D, Control Microbiology, Biological Quality Control. Consulted, analyzed and communicated results on laboratory experiments including animal studies in basic research, assay development, assay validation, assay transfers, parallel studies in testing laboratories.

Continuous Process Improvement Resource Team Member
Biometrics Research CPI Area Team Member

IV. NON-MERCK EMPLOYMENT HISTORY

<u>Title</u>	<u>From - To</u>
Senior Research Biostatistician I and II, Marion Merrell Dow Inc.	1987-1992
Instructor, Northern Kentucky University, Dept. of Mathematical Sciences	1986-1987
Consultant, Research Assistant, & Teaching Assistant, Virginia Polytechnic Institute University and State University	1980-1985
Research Assistant, National Economic Development Authority of the Philippines	1979

V. ACADEMIC EXPERIENCE

Instructor, Northern Kentucky University Department of Mathematical Sciences Highland Heights, Kentucky	1986-1987
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VI. ACADEMIC AND PROFESSIONAL HONORS

Phi Kappa Phi Honor Society
Mu Sigma Rho National Statistical Honor Fraternity
Pi Mu Epsilon Mathematical Honor Fraternity

VII. SOCIETY MEMBERSHIPS/ PROFESSIONAL ACTIVITIES

American Statistical Association
 American Association of Pharmaceutical Scientists
 PhRMA Statistics Expert Team
 Statistical Consultant to the USP Panel on Particle Count Reference Standard
 Session Chair: The Twenty-First Annual Midwest Biopharmaceutical Statistics
 Workshop (1998)
 Program Co-chair: The Twenty-Second Annual Midwest Biopharmaceutical Statistics
 Workshop (1999)
 Certified Zenger Miller Trainer

VIII. PUBLICATIONS

- SENDERAK, E.T.***, Bonsignore, H., and Mungan, D. (1993).
 Response Surface Methodology as an Approach to Optimization of an Oral
 Solution.
Drug Development and Industrial Pharmacy, Vol. 19 (4), pp. 405-424.
- Mellott, M.J., Ramjit, D.R., Stabilito, I.I., Hare, T.R., ***SENDERAK, E.T.***, Lynch, J.J.,
 Gardell, S.J. (1995).
 Vampire Bat Salivary Plasminogen Activator Evokes Minimal Bleeding Relative to
 Tissue-Type Plasminogen Activator as Assessed by a Rabbit Cuticle Bleeding Time
 Model.
Thrombosis and Haemostasis, Vol. 73 (3), pp. 478-483.
- Barrington, R.E., Subler, M. A., Rands, E., Omer, C. A., Miller, P.A., Hundley, J.E.,
 Koester, S.K., Troyer, D.A., Bearss, D.J., Conner, M.W., Gibbs, J.B., Hamilton, K.,
 Koblan, K.S., Mosser, S.D., O'Neill, T.J., Schaber, M.D., ***SENDERAK, E.T.***, Windle,
 J.J., Oliff, A., and Kohl, N.E. (1998).
 A Farnesyl Transferase Inhibitor Induces Tumor Regression in Transgenic Mice
 Harboring Multiple Oncogenic Mutations by Mediating Alterations in Both Cell Cycle
 Control and Apoptosis. Molecular and Cellular Biology, Vol. 18, No. 1, pp 85-92.
- Omer, C.A., Chen, Z., Diehl, R.E., Conner, M.W., Chen, H.Y., Trumbauer, M. E.,
 Gopal-Trutter, S., Seeburger, G., Bhimnathwala, H., Abrams, M.T., Davide, J.P., Ellis,
 M.S., Gibbs, J.B., Greenberg, I., Hamilton, K., Koblan, K.S., Kral, A.M., Liu, D., Lobell,
 R.B., Miller, P.J., Mosser, S. D., O'Neill, T.J., Rands, E., Schnaber, M.D., Senderak, E.
 T., Oliff, A., and Kohl, N. E. (2000).
 Mouse Mammary Tumor Virus-Ki-rasB Transgenic Mice Develop Mammary
 Carcinomas That Can Be Growth-inhibited by a Farnesyl:Protein Transferase Inhibitor.
Cancer Research, Vol. 60, pp 2680-2688.
- Pikounis, V. B., Antonello, J. M., Moore, D., Senderak, E. T., and Soper, K.M. (2001).
 Practicing What We Preach: The Application of Continuous Improvement in a
 Preclinical Statistics Department at a Pharmaceutical Company. Journal of Official
 Statistics, Vol. 17, No. 1, pp 187-206.

CURRICULUM VITAE

STAN ALTAN

ADDRESS: 1917 Arlington Ave **Tel:** (908) 297-1140 (H)
North Brunswick, NJ 08902 (908) 704-4083 (W)

EDUCATION: 1968 B.S. (Agriculture) Rutgers University, New Brunswick, NJ
1974 M.S. (Biometrics) Temple University, Philadelphia, PA
1977 Ph.D. (Biometrics) Temple University, Philadelphia, PA

EMPLOYMENT:

1/02–Present **J&J Pharmaceutical R&D, LLD** Raritan NJ 08869
Senior Research Fellow – Non-Clinical Biostatistics
Statistical consultant to non-clinical and preclinical R&D groups in Chemical and
Pharmaceutical Development, Biologics and Manufacturing Groups

11/86-12/01 **R.W. Johnson Pharmaceutical Research Institute**
Raritan NJ 08869
5/96-12/01 Research Fellow - Preclinical Biostatistics
Statistical consultant to preclinical R&D groups in Pharmaceutical
Development, Biotechnology, Drug Safety Evaluation
7/94- 5/96 Director, Preclinical Biostatistics
Managerial and Technical responsibilities in areas of Drug
Discovery, Pharmaceutical Development, Drug Safety, Drug
Metabolism, Biotech and Clinical Pharmacology (CNS,
Dermatology, Analgesia)
1/93- 7/94 Associate Director, Preclinical Biostatistics
Responsibilities same as above
8/90- 1/93 Assistant Director, Preclinical Biostatistics
Responsibilities same as above without Clinical Pharmacology
11/86- 8/90 Manager, Preclinical Biostatistics
Managerial and Technical support to Scientific Programming,
Drug Discovery and Pharmaceutical Development

1/86-10/86 **Wyeth Laboratories, Radnor, PA**
Assistant Director of Biostatistics
Design/Analysis of Phase III Clinical Trials – cardiovascular, CNS

9/80-12/85 **Ives Laboratories, New York, NY**
Senior Biostatistician & Assistant Director
Design & Analysis of Phase III Clinical Trials - cardiovascular area.

9/71-8/80 **Temple University, Philadelphia, PA**
1/79-8/80 Adjunct Assistant Professor, Statistics Department
Teaching introductory-level Statistics courses

EMPLOYMENT (continued) :

- 7/77-12/78 Assistant Professor, Biometrics Department
Teaching, Statistical Consultant to Medical Departments
(Microbiology, Physiology, Pharmacology)
- 9/71- 6/77 Biostatistician & Research Associate, Biometrics Department
Teaching, Computer Programming, Statistical Consultant
- 8/68- 8/71 **Armour Food Research Center, Oak Brook, IL**
Statistician Design & Analysis of experiments related to Food
Technology R&D, Sensory Evaluation, Quality Assurance,
Computer Programming.

PUBLICATIONS

- LeBlond,D., Schofield,T. and Altan,S., "Revisiting the Notion of Singlet Testing Requirements",
Pharmaceutical Technology, 2005, Vol. 29, No. 4
- Altan,S. and Raghavarao,D., "Serially Balanced Designs for Two Sets of Treatments", Journal of
Biopharmaceutical Statistics, 2005, Vol. 15, No.2
- Shoung,J., Altan,S. and Cabrera,J., "Double Bootstrapping a Tolerance Interval", Journal of
Biopharmaceutical Statistics, 2005, Vol. 15, No.2
- Altan,S., Manola,A. Pandey,R. Troisi,J., "A Statistical Design Consideration in Robotic Systems" Drug
Information Journal, 2004, Vol. 38, No.3
- Altan,S. and Raghavarao,D., "A Note on Kinetic Modeling of Stability Data", Journal of
Biopharmaceutical Statistics, 2003, Vol. 13, No.3
- Altan,S. and Raghavarao,D., "A Heuristic Analysis of Highly Fractionated 2ⁿ Factorial Experiments",
Metrika, 2003, Vol. 58
- Altan,S., Davidian,M., Manola,A. and Raghavarao,D., "The Constrained Four Parameter Logistic
Model", Dev. for Biological Standardization, 2002, Vol.107
- DeWoody,K.L. and Altan,S., Matrix Designs in Stability Studies. Recent Advances in Experimental
Designs, Nova Science Publishers, (Ed: S. Altan and J. Singh), 87-94, Huntungton, NY 2001
- Altan,S. and Singh,J., (Co-editors) Recent Advances in Experimental Designs, Nova Science
Publishers, Huntungton, NY 2001
- Altan,S. and Raghavarao,D., "A Class of Designs using a Fold-over Hadamard Matrix for Screening
Experiments", Drug Information Journal, Vol. 35, No.3, 2000

Publications (Cont'd)

DeLuca,P., Raghavarao,D., and Altan,S. "Effect of Investigator Bias on the Power and Level of the Two-Sample Z-Test", J.Biopharm Stat, Vol. 9(2) 1999

McCartney,M. A., Scinto,P.L.,Wang,S.S., and Altan,S. "Developmental Effects of Phenytoin May Differ Depending on Sex of Offspring", Neurotoxicology and Teratology Vol. 21, No. 2, 1999

Altan,S. and Raghavarao,D.: "Response Surface Methodology" Encyclopedia of Biostatistics 1998

Saranadasa, H. and Altan, S.: "The Analysis of Small-Sample Multivariate Data", J.Biopharm Stat, Vol. 8(1) 1998

Natarajan, J., Altan, S., and Raghavarao, D.: "Expiration Dating of Pharmaceutical Compounds in Relation to Analytical Variation, Degradation Rate and Matrix Designs" Drug Information Journal, Vol 31(2) 1997

Altan, S., and Raghavarao, D.: "Nested Youden Square Designs" Biometrika, Vol 83, No. 1, 1996.

Altan, S., McCartney, M., and Raghavarao, D., "Two Methods of Analyses for a Complex Behavioral Experiment" J.Biopharm Statistics, Vol. 4, No. 3, 1994.

McCartney,M. A., Scinto,P.L.,Wang,S.S., and Altan,S. "Modified Morris Maze is a sensitive indicator of impairment of learning and memory" Neurotoxicology and Teratology, Vol 16, 1994

Altan, S., and Natarajan, J.: "Using PROC NLIN to Combine Estimates of Relative Potency" SUGI17 Proceedings 1992.

Buck, R., Burch, L., and Altan, S.: "STABLE: An AF System for the Analysis of Drug Stability Systems" SUGI 14 Proceedings, 1989

Altan, S.: "PBS: An Intelligent Statistical Analysis System", SUGI 13 Proceedings, 1988

Altan, S.: "Regression to the Mean - a Review of the Literature" J. of Sensory Studies, Vol. 2, 1987

Altan, S.: "Use of Life Table Methods in Estimating Incidence of Adverse Reaction Due to a Drug" Pharmacoepidemiology Newsletter, Vol. 1 No. 2/3, 1986

Chiasson M.A., and Altan S.: "Misuse in Statistics." The New York Statistician, Vol. 36 #3 1985

Weiss W., Altan S., Rosenzweig M.: "Prognostic Factors in Lung Cancer" Medicine/Genesis, Vol. 2, No. 2, Winter 1976

Weiss W., Altan S., Rosenzweig M.: "Lung Cancer Type in Relation to Cigarette Dosage" Cancer, Vol. 39, No. 6, June 1976

Publications (Cont'd)

Gacula M.G., Altan S., and Kubala J.: "Data Analysis using Paired Designs" J. of Food Science, November 1971

Presentations

"A Case Study of the Bayesian Approach to Constructing Tolerance Intervals for the 1-Way Random Effects Model" Oscar Go, Jyh-Ming Shoung, Stan Altan, Midwest Biopharmaceutical Statistics Meeting, Muncie, IN May 23, 2007

"Asymmetry in the Dose Response Curve in Relation to the 4-parameter Logistic Model". S. Altan, M. Davidian, A. Manola, O. Go, XXIIIrd International Biometric Conference, Montreal, Canada. July 18, 2006

"An Application of Serially Balanced Designs for the Study of Taste Samples with the α -ASTREE Electronic Tongue", S. Altan, A. Manola, Y. Shen, 2006 International Conference on Design of Experiments and Its Applications, Tianjin, China, July 14, 2006

"Use and Misuse of the Gage R&R Study ", S. Altan, A. Manola, J. Shoung, Midwest Biopharmaceutical Statistics Meeting, Muncie, IN May 23, 2006

"Statistical Design and Analysis of Excipient Compatibility Studies", Second Annual Conference on Drug-Excipient Compatibility, Institute for International Research, Chaired by R.N. Pandey, Princeton NJ, March 21, 2006

"Double Bootstrapping A Tolerance Limit", International Chinese Statistical Association 2005 Conference, Washington DC, June 15, 2005

"Statistical Design and Analysis of Excipient Compatibility Studies", Conference on Drug-Excipient Compatibility, Institute for International Research, Chaired by R.N. Pandey and H.G. Brittain, Princeton NJ, September 22-23, 2004

"Laboratory-to-Laboratory Reproducibility of Viscosity Measurements of a pharmaceutical suspension", Katherine DuPont, Ramendra Pandey, Timothy Gilmor, Stan Altan and Areti Manola, Eastern Analytical Symposium, Somerset, NJ, November 2003

"Double Bootstrapping a Tolerance Limit" PhRMA CMC Statistics Technical Expert Team Meeting, November 5, 2003.

"Modeling Issues in Potency Testing of Biologics with Emphasis on Nonlinear Modeling" – Invited Speaker to the Midwest Biopharmaceutical Statistics Meeting, Muncie, IN May 19, 2003

"Use of the Constrained Four Parameter Logistic Model in Potency Testing" – Invited Speaker to the Temple University Statistics Colloquium Series, Philadelphia, PA, October 20, 2000

Presentations (Cont'd)

"Use of the Constrained Four Parameter Logistic Model in Potency Testing" – Invited Speaker to the WHO/IABS International Workshop on the Design and Analysis of Potency Assays for Biotechnology Products, NIBSC, London, UK, October 5-6, 2000

"Matrix Designs in Stability Studies" with Kim DeWoody –Design of Experiments Conference in Honor of Professor D. Raghavarao, Fort Washington, PA, October 2, 1999

"Effect of Investigator Bias on the Power and Level of the Two-Sample Z -Test" with Paul Deluca and D. Raghavarao - The 6th Merck-Temple Conference on Research Topics in Pharmaceutical Statistics, Philadelphia PA October 23, 1998

"An Overview of Matrix Designs in Stability Studies" – Invited Speaker to 1998 Conference on Pharmaceutical Analysis (Land O'Lakes Conference), Merrimac, Wisconsin August 3, 1998

"The Use of the Anderson-Hauck Method for Interlaboratory Comparisons" with Frances Stewart and Jaya Natarajan - Midwest Biopharmaceutical Statistics Workshop, Muncie, IN May 1995

"Design and Analysis of Stability Studies" Session Organizer - PHRMA Biostatistics Subsection Conference, Washington, D.C., October 1994

"Behavioral Toxicology" Session Organizer - PMA Biostatistics Subsection Conference, Baltimore, Md, September, 1993

"Analysis of the Direct and Residual Effects of Stimuli on the Startle Reflex in Rats" - Symposium on Repeated Measurements and Cross-Over Designs, Temple University, May 1993

"Combining Estimates of Relative Potency" - SUGI 17 Meeting, Honolulu, Hawaii, April 1992

"PBS: An Intelligent Statistical System" - SUGI conference, March 1988

"An Intelligent Statistical Analysis System" - DIA Workshop, November 1988

AWARDS

1990 Phillip B. Hofmann Award for Research and Development (Johnson & Johnson Company Award to Research Scientists)

1991 Pinnacle Award, a peer driven Award for Excellence (Johnson & Johnson Award)

Internal Presentations

'Statistics of Bioassay' for GBSC lab personnel, September 11, 2006, Raritan, NJ

"A Bioassay Calibration Application of the Slope-Ratio Method" (Poster given at 8th J&J Pharma Statistics Conference, Raritan, NJ) S. Altan, O. Go, A. Manola, P. Niven

"Bayesian Approach to the calculation of Tolerance Intervals", Oscar Go, Jyh-Ming Shoung, Stan Altan, 8th J&J Pharma Statistics Conference, September 19, 2004

"OOS Testing" Annual GMPS Leaders' Meeting, Vacaville Ca, April 27, 2006

"Stability Modeling with a Double Bootstrap", Oscar Go, Alfred Barron, Areti Manola, Stan Altan, 6th J&J Pharma Statistics Conference, Princeton, NJ, September 30, 2004

"Statistics in Specification Setting" The 5th J&J Pharma Statistics Conference, Princeton, NJ, September 25, 2003.

"Introduction to Statistical Design of Experiments and the use of ECHIP[®]" with John Mills – In-house course taught to PRI scientists in Chemical Development, Raritan NJ, July 13, 2000

Other Relevant Professional Experience

Facilitator for PERI Sponsored Preclinical Statistics Course 3/12/95-3/14/95

Statistical Consultant to CNS clinical studies for Merck & Co. (1978)

Statistical consultant to American Hoechst, Open label Antibiotic Trials (1977)

Expert Witness to US Justice Department (1979)

Affiliate Professor at Temple University, Statistics Department (current)

Invited Editor for Special Issue on Non-Clinical Pharmaceutical Statistics, J. of Biopharmaceutical Statistics, (2005) Vol 15, No.2

Session organizer on Non-Clinical Applications in the Pharmaceutical Industry, International Chinese Statistical Association 2005 Conference, Washington DC, June 15, 2005

Associate Editor, J. of Biopharmaceutical Statistics (2005-current)

Member of PhRMA CM&C Statistics Experts Team, 2003-current, member of various subcommittees

Elected member of PhRMA Biostatistics and Data Management Technical Group, 2004-current

Professional Vitae

ROWLAND ANDERSON YOVONIE, Ph.D. PE

6 Heather Lane
Middlesex, New Jersey 08846
732-271-8998

Hoffmann La-Roche Pharmaceuticals
Nutley, New Jersey 07110
(973)-235-2331

EDUCATIONAL BACKGROUND:

Earned the Bachelor's and Master's degrees from Iowa State University, Ames Iowa, in Industrial Engineering. Pursued the Ph.D. program in Industrial Engineering, with emphasis in Reliability Engineering, Applied Statistics and Quality Systems at Oklahoma State University, Stillwater, Oklahoma, and earned the Ph.D. in Engineering from California Coast University, Santa Ana, California.

DISSERTATION:

"Economic Design of Interrelated Attributes Acceptance Sampling Plans in Multistage Production Systems".

PROFESSIONAL ASSOCIATIONS/CERTIFICATIONS

- A registered Professional Engineer (PE) in Quality Engineering, in the State of California
- An ASQ (American Society for Quality) certified Six Sigma Black Belt
- ASQ Certified Reliability Engineer (CRE)
- ASQ Certified Quality Engineer (CQE)
- ASQ General Member
- J&J Certified Six Sigma Black Belt

SUMMARY AND ACCOMPLISHMENTS:

Twenty-four years of experience in Design and Process Excellence Applications, Quality Systems, and FDA Regulatory Submissions in the Medical and Pharmaceutical industries. Thirteen and half years dedicated to leading, developing, implementing, promoting, managing, mentoring, and teaching Design Excellence, Process Excellence, Design Control, Failure Analysis, and Validation programs within the Medical Device and Pharmaceutical industries.

- Developed and established a Design Excellence program for Cordis, a Johnson & Johnson Company, and facilitated process improvements within Cordis global workplace. Provided Reliability Engineering training to Cordis Associates in the USA and Europe.

- Performed Due Diligence and Quality Assurance Technology assessments for Cordis' acquisition of a Medical Device company.
- Developed, implemented and directed Ethicon Endo-Surgery Corporate Reliability program that reduced time to market by 45% and customer complaint rate by 98%.
- Designed programs to prevent and resolve FDA's 483 and Warning letter and actively participated in FDA Inspections to provide answers to complex statistical questions.
- Developed and implemented Corporate Procedures on Design Controls, Process Validation, Design Reliability, Design and Process Failure Modes and Effects Analysis (DFMEA & PFMEA), Destructive and Nondestructive Test Method Validations, Design Specifications, Statistical Techniques and Quality Systems for Contract manufacturing.
- Developed and led a high performance quality organization charged with ownership of Endovascular product family quality/reliability and responsibility to champion customer quality focus in activities with New Product Development (NPD) and Regulatory Affairs. Established departmental goals, objectives and developed annual departmental expense/capital budgets, and allocated resources to complete multiple projects within scheduled time.
- Provided the departments, and the Cordis organization as a whole, with leadership in developing, implementing, and managing Design Assurance Systems. Formulated and directed all aspects of Design Assurance programs to embrace R&D, Operations and Contract Manufacturing.
- Developed training materials and trained managers, engineers and technicians at Ethicon Endo-Surgery, Cordis, Guidant, and at J&J Learning Services Consortium.
- Managed, mentored, and directed the professional and technical development of Associates in R & D, Operations, Quality/Reliability departments.
- Instructor at J&J Learning Services Consortium in these technical skills and fundamentals: (a) Applied Statistics & Data Analysis, (b) Designed Experiments & Process Characterization, (c) Reliability Engineering, (d) Weibull Engineering Analysis, (e) Process Capability Analysis.
- Developed and implemented a Total Quality Cost System for a Pharmaceutical company to identify, trend, and to reduce quality costs.

PROFESSIONAL EXPERIENCE:

Hoffmann La-Roche Pharmaceuticals, Nutley, New Jersey, January 2004 - Present Group Leader Quality Engineering & Statistical Support

Provides statistical support to Quality Management, Technical Operations, Pharmaceutical Research & Development clients, and, in conjunction with the Quality

Engineering & Compliance department. Using statistical software and advanced statistical techniques, provides statistical support on a timely basis to clients. Ensures compliance of projects and services with Food and Drug Administration (FDA) current Good Manufacturing Practices (cGMP), global health regulations, and Roche local and global policies and procedures.

- Leads and participates in Operational Excellence Program and cross-functional teams to develop, improve, and maintain overall quality systems, including quality standards, process control techniques, and inspection/testing plans based on FDA systems inspection model to ensure safety, reliability and efficacy of new products, processes and significant changes.
 - Leads teams and facilitates use of technical resources or Quality Reliability Engineering tools, such as risk analysis, root cause analysis, statistical process control, failure modes and effects analysis; statistical techniques such as, process capability, design of experiment, acceptance sampling, and validation testing.
 - Leads or participates in formal project management initiatives to improve products.
 - Provides coaching/facilitation of leadership to identify and accomplish necessary tasks.
 - Provides training in and leads the implementation of Operational Excellence program activities
 - Manages Operational Excellence projects, writes technical reports, standard operating procedures (SOP), and creates or updates product standards.
 - Provides technical leadership in Quality / Reliability engineering to the Roche organization.

Cordis, a Johnson & Johnson Co., Warren, New Jersey, January 2000 – Dec. 2003
Manager/Consultant/Principal Engineer, Reliability/Quality Engineering

- Championed and developed the Cordis Design Excellence (Integrated Reliability Design Assurance) program. Deployed and modeled the program on a New Product development project that resulted in a savings of \$180,000.00 in Design Verification costs. The DEX program was approved by Vice Presidents of Quality Assurance, New Product Development, Regulatory Affairs and Operations and, consequently, integrated into Cordis Franchise Product/Process Development System in 1998.
- Developed an Analytical Release Sampling Plan using the tools of DEX and PEX for a major project that would provide a cost savings of 1.5 million dollars for the first four months after its implementation.
- Provided Design and Process Excellence consulting services and training to Cordis Associates in NPD, QA, Operations and Regulatory Affairs.
- Mentored both certified Green Belts and those awaiting certification.
- Worked with Contract manufacturing to characterize, define, and optimize their processes to increase yield and reduce cost using PEX tools and practices.

Cordis, a Johnson & Johnson Co., Warren, New Jersey, June 1996 – Dec.1999
Manager Reliability/Quality Engineering – Endovascular System

- Developed and led a high performance quality organization charged with ownership of Endovascular product family quality/reliability and responsibility to champion customer quality focus in activities with New Product Development and Regulatory Affairs. Staffed, mentored, and managed the Endovascular Quality/Reliability Engineering department.
- Provided the department and the organization with leadership in developing, implementing, and managing Design Assurance Systems. Formulated and directed all aspects of Design Assurance programs to embrace R&D, Operations and Contract Manufacturing.
- Established and managed the Reliability Engineering lab responsible for testing competitive products, prototypes, and conducting Design Verification and Stability evaluations, as well as failure and root cause analyses. Established and managed Product Quality Services lab to analyze, test, and respond to customer complaints. Developed a linkage between product complaints and product failure modes observed during design verification.
- Provided failure analysis results to New Product Development teams for corrective action(s) and design optimization. Verified that corrective action(s) resulted in eliminating the customer complaint.
- Supported the development of new products and processes and provided technical and managerial competence in Design Control, Product reliability, Process Validation, Test Method Validation, Statistical Techniques, Design and Process FMEAs, and Product Complaints.
- Developed and implemented a Corporate Design Control system based on FDA Quality Systems Regulation and ISO 9001, and created appropriate procedures to ensure that individuals who affect New Product Development have received appropriate training and are in compliance. Provided guidance and technical expertise to ensure products meet applicable customer and regulatory requirements.
- Provided engineering and technical support to Product Quality Services, (Product complaints), Supplier Quality management, and Contract Manufacturing.
- Provided technical support/direction to Operations, Contract Manufacturers and New Product Development in the areas of Design of Experiments, Quality Systems Development, Process Failure Modes and Effects Analysis, and Process Characterization and Capability Analysis.

Ethicon Endo-Surgery Inc. Cincinnati, Ohio, August 1994 – June 1996
Staff Reliability Engineer / Consultant

- Developed reliability test models to assess the reliability of the device design for all project teams in R&D for Endoscopic Surgical devices.
- Developed Corporate Reliability Procedure documentation to define the Ethicon Endo-Surgery practices for the development and assessment of device reliability in compliance with ISO 9001 and Pre-Production Quality Assurance (PPQA).
- Developed and implemented Design Reliability activities (modeling, allocation, prediction, reliability growth and demonstration) into Ethicon Endo-Surgery New Product and Process Development system.

- Presented device reliability data to senior management for readiness review. Provided consulting services to New Product Development, Surgical R&D, Team Quality, and Operations Associates in the areas of Design Reliability, Weibull Analysis, Supplier Component Reliability, and Applied Statistics. Championed the application of Reliability Engineering in device design and development.
- Developed training materials and trained design, development, quality, process, and manufacturing engineers in Reliability, Weibull Engineering Analysis, Statistics, Quality System, Process Capability Analysis, and in Design Failure Mode and Effects Analysis (DFMEA).

Advanced Cardiovascular Systems, Inc. Santa Clara, CA. Feb. 87 - August 1994
Senior Reliability Engineer II/Supervisor, Material Technology (Jan. 1992 - Aug. 1994)

- Developed new test methodologies for evaluating new balloon materials (polymers) for Angioplasty Dilatation catheters. Established a test laboratory to support R&D for testing components, subassemblies and finished device. Organized and supervised the activities of one engineer, one senior technician, and four technicians in the R&D test laboratory.
- Applied the techniques of Design of Experiments to reduce variations in the extrusion processes during the development of new balloon materials.
- Evaluated material characteristics of and the effects of irradiation processes on new extruded polymers to identify design deficiencies and to provide engineering recommendations for corrective action.
- Developed training materials and trained R&D engineers and technicians in Applied Statistics, Process Capability Analysis and Process optimization.

Senior Reliability Engineer II/Supervisor (Feb. 1987 - Dec. 1991)

- Supervised Reliability laboratory, two engineers, and three senior technicians.
- Developed and implemented a formal Design Review Process for R&D in designing and developing cardiovascular devices.
- Developed Fault Tree Analysis (FTA) for Electro-Mechanical Cardiovascular devices.
- Developed and implemented a formal Failure Mode, Effects and Criticality Analysis for Dilatation catheters.
- Worked with R&D and manufacturing engineers to facilitate the application of device development and design review techniques such as FMEA, FTA, Quality Function Deployment (QFD), Variation Analysis (VA), and Design for Manufacture and Assemble (DFMA), to ensure device and process reliability at the lowest cost.
- Developed FDA filing test protocols and conducted tests in support of IDE, 510K, PMA submissions and approvals. Analyzed test results and provided a written subsection to Regulatory Affairs for FDA submission.
- Developed clinical test protocol and data analysis.
- Presented device reliability analysis in design review in line with PPQA and FDA's guideline.
- Wrote reliability specifications, standard test methods (STMs) and approved engineering change orders.
- Provided statistical consulting services to Reliability, Quality, R&D, Regulatory Affairs, Market Research and Clinical Research departments.

- Developed and implemented a corporate reliability programs for cardiovascular devices.
- Trained R&D engineers, technicians, and manufacturing engineers in Applied Statistics.
- Reviewed FDA guidelines for Angioplasty Dilatation Catheters and establish statistical rationale and protocol to reduce device sample size to one-third of the sample size originally recommended by FDA.
- Established a statistically valid patient sample size based on proportional statistics for success/failure criteria.

Kendall McGaw Laboratories Inc., Irvine CA. April 1986 - Feb. 1987

Senior Quality Engineer

- Conducted statistical studies for processing of medical devices based on tolerancing and device specifications.
- Designed, implemented and maintained statistical process control (SPC).
- Perform process capability analysis.
- Provided quality engineering support for Computer Integrated Manufacturing and develop test methods to evaluate device quality.

Boehringer Ingelheim Pharmaceutical Inc. April 1985 - March 1986

Quality Engineer

- Planned, designed, implemented and maintained a Total Quality Costs system for the design, development and manufactured of hypertensive drugs.
- Performed quality costs analyses and established systems to evaluate and reduce quality costs.
- Organized quality costs information system to provide management with necessary data to make meaningful quality decisions.
- Provided training in Statistical Process (SPC) and Quality (SQC) Control to Production and Quality Control departments.
- Audited and reviewed existing inspection and test methods for areas of improvement.
- Provided Quality Engineering support for new and existing process validation.
- Performed audits, surveys and vendors qualifications.

Baxter Travenol Laboratories Inc. Mtn. Home, Arkansas; Sept. 1983 - April 1985

Quality Assurance Engineer

- Optimized production processes for Fenwal bags and cannulas.
- Validated new and existing production equipment.
- Designed developed and implemented new inspection and sampling techniques.
- Developed and implemented Statistical Process Control (SPC) on injection molding extrusion, aseptic filling and induction heating processes.

Myron B. Diener

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Residence

956 East 1st Street
Peculiar, MO 64078
(816) 779-5640
mbdiener@comcast.net

Education & Certifications

M.S. Statistics (GPA 3.81)
December, 1988

Oklahoma State University
Stillwater, Oklahoma

B.A. Mathematics (GPA 3.80)
December, 1981

Goshen College
Goshen, Indiana

American Society for Quality (ASQ)
December 2003

Certified Quality Engineer (CQE)

Course Work

Statistics: Introduction to Probability Theory and Statistical Inference, Theory of Linear Models, Theory of Sample Designs, Statistical Methods, Applied Regression Analysis, Experimental Design, Time Series Analysis, and Advanced Experimental Design.

Mathematics: Modern Algebra, Differential Equations, Linear Algebra, and Principles of Analysis, Integral Calculus – 3 semesters.

Electronics: Direct Energy Conversion, Introduction to Solid State Electronics.

Work Experience

sanofi-aventis: 1997 – present

Consulting Statistician

Training: Lead trainer on statistical methods related to the use of Discoverant exploratory analysis software. Led site quality engineers through training to complete CQE. Several courses developed and delivered on utilization of SAS/JMP for exploratory data analysis.

Programming: Develop, test, and implement a sequence of SAS programs to estimate product release limits based on the *Random Slopes* methodology.

Consulting: Design Statistical Experiments to meet the learning objective of manufacturing engineers. Develop Statistical Models on observational data to assist in explaining product quality problems as functions of raw material characteristics, and processing conditions.

Management: Provide direction and manage the activities of an intern statisticians. Train and direct new associate on methods and use of Stability Analysis System.

Publication: "Development of a Content Uniformity Test Suitable for Large Sample Sizes," Drug Information Journal (August 2006).

Baker University: 2000

Adjunct Instructor

Courses taught: Quantitative Analysis (OR), College Algebra

Myron B. Diener

The Associates: 1996-1997 (contract) **SAS Programmer/Application Developer**

Programming: Developed a new data model to facilitate summarization, and estimation of Customer Retention within and between business divisions. Extensive use of SAS data step, associated procedures (i.e. sort, transpose, summary, . . .) and SAS macro language. Dealt with very large databases (> 100k records) in building these summaries.

Consulting: Worked with internal business customers to define appropriate business reports to facilitate support in key business management decisions. Consulted with internal clients on interpretation of these reports, both ad hocs, and monthly production reporting.

Cornerstone Associates: 1992 - 1996 **Quality Assurance Systems Statistician**

Analysis: Process Capability Studies, Observational Studies, and Designed Experiments to support setting up Statistical Process Control in continuous manufacturing processes.

Training: Statistical training to operators, managers and engineers to support Statistical Process Control and Experimental Design. Developed 2-day SPC course, and 6-day DOE Courses for clients. Delivered Team Member, Leader and Facilitator training to client sites

Management: Facilitate through steering and project team members the process of implementing process stability methods in the manufacturing operation. This includes: Procedure Control, Supplier Quality Control, Formulation Control (set-up control) as well as Statistical Process Control and Robust Process Design.

Wynn's Climate Systems Inc.: 1992 **Quality Manager**

Management: Supervised 2 Quality Engineers and 5 Quality Auditors.

Leader of 3 Quality Improvement Teams which met weekly to develop and monitor project activity with the objective of optimization and variation reduction of these manufacturing processes.

Training: Conducted weekly Technical Training sessions with the Quality Engineering group (5 individuals). Topics covered include: 1) Basics of Probability Theory, 2) Acceptance Sampling Theory and Applications, 3) Statistical Hypothesis Testing, 4) Elementary and Advanced Statistical Process Control, and 5) Statistical Experimental Design for Quality Improvement.

D & S Plastics International: 1990 - 1992 **Industrial Statistician**

Training: Led a team that developed and conducted basic SPC training for manufacturing personnel. Developed and conducted training on product capability and the meaning of Capability Indices for the management staff. Developed and conducted training on conducting Process Capability Studies, Regression Modeling, and Statistical Experimental Design for the Process Engineering and Product Development groups.

Analysis: Developed an analysis plan for capability studies on the production lines. Developed software (written in SAS) to generate summary statistics from the data streaming from the production floor. Supported the continuous improvement of the compounding and injection molding processes through design, analysis, and interpretation of experiments.

Myron B. Diener

Management: Membership on the Steering Team to implement SPC on the production line. Subsequent membership on the Quality Management Team to implement SPC throughout the whole organization. Participation in Process Capability and Raw Material diagnostic teams for evaluation of input factors influence on final product characteristics.

Trilogy Consulting (Monsanto): 1989 - 1990

Project Statistician

Programming: Edited existing and Authored new SAS programs to provide summary statistics (means, std., cv, . . .) on a periodic basis for drug stability data.

Analysis: Interpreted FDA requirements for estimating drug shelf-life by extrapolating a 1st degree linear model with the appropriate prediction interval. Utilized SAS REG and GLM procedures to obtain these estimates from existing historical data.

Developed non-linear (Arrhenius) models to incorporate accelerated testing data into the model for prediction of shelf-life. Utilized SAS NLIN procedure to obtain parameter estimates for these models. Consulted with the Bio-stat group on the analysis and modeling of drug stability data.

Advanced Micro Devices: June - Aug., 1988 (summer intern)

Intern Statistician

Designed and analyzed of fractional factorial experiments for process optimization. Developed a model to support acceptance decisions for incoming photomasks. Consulting with and training of engineers on experimental design and data analysis.

OSU Statistics Dept.: 1986 - 1988

Graduate Teaching Assistant

Taught elementary and intermediate statistics courses.

Earlynn Electronics: 1983 - 1985

Electronic Technician

Troubleshooting, repair, and design of electronic printed circuit boards.

Lustre Christian High School: 1982 - 1983

Math Teacher

Teaching secondary Mathematics and Physical Education. Head Coach for Cross Country, Basketball, and Track.

Computer Experience

Software: SAS, SAS-JMP, Statgraphics, ECHIP, Statistica, S-Plus, TEX & LaTeX, Excel, Access, WORD, Power Point

Operating Systems: Windows, UNIX, VMS, CMS, MS-DOS

Programming languages: Basic, FORTRAN, Pascal

Organizations/Societies

ASQ: American Society for Quality – Certified Quality Engineer

Hobbies

Soccer Coach, Tennis, Weight Lifting, Running, Skiing, Flying, Lawn Care, Commodity Trading

References and additional information will be made available upon request

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SYNOPSIS OF RESUME OF: JIM PAZDAN

JOB OBJECTIVE

Applied statistician involved with statistical consultation, design of experiments, statistical analysis, scientific programming, statistical education, and general statistical problem solving in an applied research or engineering environment.

SUMMARY OF QUALIFICATIONS

Work experience as a statistician and as a statistical consultant for several major firms. Strong academic background in statistics and strong applied computer skills. Extensive experience working very closely with chemists, biologists, pharmacists, engineers, and MD's. Three years industrial experience as an electronic technician.

EXPERIENCE

(Oct 2000 to present) Senior Principal Statistician **supporting** Pharmaceuticals R&D, Analytical Chemistry, and misc. non-clinical activities at Novartis Pharmaceuticals Corp. in East Hanover, NJ.

(Feb. 88' to Sep 2000) Senior Research Biostatistician supporting Pharmaceuticals R&D, Chemical Processing, Analytical Chemistry, general nonclinical, and pre-clinical (animal studies) at Bristol-Myers Squibb in New Brunswick, N.J.

(Jan 86' to Jan 88') Statistician in the Technical Dept. at Consumers Union (publisher of Consumer Reports) in Mt. Vernon, N.Y.

(June 1984 to Jan 86') Statistician in the R&D Biometrics Dept. of Revlon Health Care in Tuckahoe, N.Y.

(April 1983 to June 84') Statistical consultant through Trilogy Consulting Corp. The three major clients were G.D. Searle in Skokie, Ill., Baxter Travenol in Morton Grove, Ill., and Abbott Labs (Pharmaceutical Products Division) in Abbott Park, Ill.

(Summer 1982) Statistical consultant at Abbott Labs, Hospital Products Division in Abbott Park, Ill.

(1976 to 1982) Contract and temporary work as an electronic technician for various companies (3 years cumulative)

COMPUTER SKILLS

Proficient in SAS, EXCEL, GAUSS, and APL. Strong experience with Visual Basic, VBA in Excel, basic HTML web page writing, FORTRAN, SAS's IML matrix language, and C. Use GAUSS, SAS (for DOS, Windows NT, and for OS/2), Statgraphics, EXCEL, APL, and VB on Window based PC's. Recent Oracle/SQL experience in writing nested queries and using them in SAS's SQL procedure. Used MVS, CMS, and TSO on IBM mainframes, and VMS on VAX computers. Used APL and C on a UNIX system (familiar with Unix Shell programming).

EDUCATION

M.S. (August 1983) in Applied Probability and Statistics. Northern Illinois University.
B.S. (August 1979) in Psychology, minor in Statistics. Illinois Institute of Technology.

EXPERIENCE**Oct 2000 to Present:**

Novartis Pharmaceuticals Corporation, Work in Pharmaceutical Development, supporting Pharmaceuticals R&D, Analytical Chemistry, and general non-clinical statistics in East Hanover, N.J.

1) Sole statistical support person for Pharmaceutical Development, Analytical Chemistry, and miscellaneous groups in Technical Development. Consult with Drug Safety and Chemical Development. Consult with parallel groups in Basel, Switzerland and frequently collaborate with their own sole statistician.

2) Developed classes in basic statistics, design of experiments, linear regression, stability analysis, and other useful topics. Taught classes to a majority of the formulators and analytical chemists. Introduced and provided instruction in Statgraphics, which provides an alternative to Excel worksheets for use in experimental design and basic statistics.

3) Provide frequent experimental designs to Pharmaceutical Development formulators for all phases of formulation development. Formulators mostly use pre-programmed Excel workbooks with experimental designs ranging from 3 to 8 experimental variables. Experiments involve general formulation robustness, improvement of content uniformity, tablet compression, enhancement of product stability, improvement and robustness of dissolution, etc. Started the use of Statgraphics for use in more flexible experimental designs than are available on the Excel workbooks. Researched methods to do screening designs without the need for replicates and provided Excel tool. Presented approach at 2003 ASA national meeting.

4) Developed GMP validated SAS programs to determine product stability shelf life that is used throughout Novartis development sites world wide. Contracted SAS Institute to do the SAS programming, who used the SAS algorithms that I provided them for model building. Assisted in validating the programs, gave instructions in its usage at multiple Novartis worldwide sites. Working on improvements for next version using SAS 9.1. Also, provide general support and training in the analysis of stability studies.

5) Working with Analytical R&D, Pharmaceutical Development, and Chemical Processing on our new PAT initiatives. Work with the analysis of primarily NIR data using PLS regression techniques. Developing Excel and SAS tools for specialized diagnostic plots and statistical tests. Working on an international team that has a CRADA with the FDA to use design space methodology for an existing product. Heavily involved with designing experiments through out the drug product and drug substance steps in order to define the design space(s). Project is scheduled to finish in 4Q 2007.

6) Developed Excel and SAS tools for use by formulators and chemists to solve problems such as sieve analysis, microscopic particle size analysis, assay linearity, experimental designs and analysis, "best case" content uniformity estimation using particle size, etc. Statistical tools are available on the company intranet, along with other useful information. Serve as web master for department.

7) Developed an innovative Excel workbook tool to evaluate "batch risk" of passing process specifications for common USP release tests and other required specifications. Tests use available validation and production scale batch data and compute probabilities with confidence limits of passing criteria for future batches. Variance component with confidence interval techniques are used.

Statistical and Computing techniques used: linear regression, design of experiments, analysis of variance, variance component estimation and confidence intervals, density estimation, partial least squares, etc. Use SAS for Windows, Excel, VBA for Excel, Visual Basic

6.0, SQL (SAS and in Excel) on IBM PC's. HTML web authoring on Windows and Unix based servers.

EXPERIENCE (CON'T)**February 1988 to Sept, 2000:**

Bristol-Myers Squibb, Biostatistics and Data Mgt. Dept., supporting Pharmaceuticals R&D, Chemical Processing, general nonclinical, pre-clinical (animal studies), and Analytical Chemistry in New Brunswick, N.J.

1). Design and analysis of process studies (scale up and optimization) for Pharm. R&D. using factorial, central composite, split plot and other designs. Experiments involve formulation robustness, slow release dissolution, tablet compression, enhancement of product stability, etc.
2). Statistical analysis for Pharmaceuticals R&D of various product stability studies from exploratory to Phase III NDA. Nonlinear modeling of accelerated (high temperature/humidity/pH) stability studies. Recommend release limits for products based on estimated product stability and assay variability. Interact with regulatory reviewers from different countries concerning stability analyses. Received "Compliments of Squibb" award (6/90) from Pharmaceuticals R&D for expedient work on a product's stability analysis which obtained full shelf life approval from the Canadian Review Board.

Programmed SAS programs, using SQL, to query the large Oracle stability databases in order to provide customized stability reports for review by the formulators.

3) Extensively involved with Chemical Processing with designing and analyzing process and scale up studies for maximizing yield and purity and minimizing unwanted byproducts.

Programmed an extensive set of Excel workbooks that will do the design and analysis of 2 level factorial designs, large screening factorial designs, central composite, and misc. innovative statistical designs. The Excel workbooks are posted on a Web page that are accessible through the company's intranet. Maintain the Web pages using HTML and post examples of experiments done by the chemists, as well as organize all of the educational training materials and courses. Developed, with the input of statisticians in our group, training courses in DOE and taught the courses at several BMS sites to groups of chemists. Actively involved in developing further education and training approaches in order to reach out to more of the chemists in BMS; e.g. training select chemists more extensively in DOE ("specialists") that would be able to effectively consult with other chemists in DOE. Also involved in developing new methodologies to design and analyze studies for: a) optimizing crystallization, b) combinatorial chemistry, c) fermentation processes, and d) basic kinetics modeling (developing Excel workbooks).

4). Analyze large animal cancer studies for the Pathology department using time adjusted Peto analysis in conformance with FDA and GLP guidelines. Developed SAS programs to do extensive database checking and automated analysis using the client's cancer database. Co-authored a published paper for an exact permutation test for testing of linear trend in animal cancer studies; programmed the permutation calculations in FORTRAN. In the process of writing and validating a new Peto analysis routine using SAS's IML procedure to be used for all future cancer studies.

5). Design and analysis of assay validation (precision, accuracy, and linearity) for Analytical Chemistry as well as comparison of assay methods. Developed and programmed an assay validation software package in GAUSS which run on their IBM PC's.

6). Designed a statistical quality assurance system to assure nearly error free filling of clinical supplies for Pharm. R&D that exceeds Six Sigma quality - $< 1/3.4$ million defects (misfills) per opportunity.

7) Analyze some toxicology studies requiring non-standard methodology. Provided a statistical module for use in a new automated toxicology system and help validate it.

8). Nonlinear modeling, optimization, and basic research with dynamic light scattering used to obtain particle size distributions of sub micron particles using state of the art laser and digital equipment. Provide innovative statistical modeling and support for other advanced instrumentation.

Statistical and Computing techniques used: linear and nonlinear regression, design of experiments, analysis of variance, variance component estimation and confidence intervals, response surfaces, nonparametric techniques, exact permutation tests, etc. Use SAS (for DOS, Windows, NT, and for OS/2), EXCEL, Visual Basic, VBA for Excel, APL, and MATHEMATICA on IBM PC. Use FORTRAN on OS/2. Experience with SQL to directly query complex stability databases stored in Oracle. Used SAS and FORTRAN on IBM mainframes.

(Continued)
(EXPERIENCE (CON'T))

January 1986 to January 1988:

Consumers Union (publisher of Consumer Reports), Technical Dept.,
Mt. Vernon, N.Y.

- 1). Consulted on statistical design for testing on a variety of consumer products. Involved with chemical, electronic, and engineering projects, as well as food sensory evaluations and some survey work.
 - 2). Statistically analyzed data from clients' projects and prepared statistical reports for the Technical Dept. Reviewed statistical aspects of its magazine articles with the Editorial Dept.
- Statistical and Computing techniques used:** special large incomplete block designs, linear models, multiple comparisons, probability density estimation, clustering techniques, logistic regression, etc. Use of SAS as well as extensive use of APL and C on a Unix system workstation.

June 1984 to January 1986:

Revlon Health Care [USV], R&D Biometrics Group, Tuckahoe, N.Y.

- 1). Statistical analyses and reports provided for a wide variety of clinical pharmacology studies such as pharmacokinetics, pulmonary function, hemodynamics, and special population studies. Designed and analyzed numerous bioavailability studies. Designed and wrote a complete statistical system to analyze teratology studies.
 - 2). Led statistical task force in developing statistical methodology in the area of multiple comparisons in unbalanced multifactor clinical studies. Researched the mathematical structure and its implication of least squares solutions for treatment comparisons in highly unbalanced models.
- Statistical and Computing techniques used:** Parametric and nonparametric analyses, linear models, multiple comparisons, power calculations, Bayesian methodology, Monte Carlo simulations, survival analysis, etc. Extensive use of SAS and some FORTRAN on a IBM mainframe using TSO.

April 1983 to June 1984:

Statistical consultant through Trilogy Consulting Corp. at Abbott Labs, Pharmaceutical Products Division, Abbott Park, Ill. from January to June 1984. Provided statistical analyses and SAS programming support for clinical efficacy indications of hypertension, angina, and arrhythmia. Consulted in statistical summarization of the efficacy results for a NDA submission.

(April 83' to January 84')

Statistical consultant through Trilogy Consulting Corp. at G.D. Searle in Skokie, Ill. and briefly at Baxter Travenol Labs in Morton Grove, Ill.

- 1). Developed parametric variance component methodology to be used as criteria for determining "positive" and "negative" carcinogenic responses of test compounds in unscheduled DNA synthesis studies. Involved in planning of future experimental designs.
- 2). Statistical analysis of large historical database for development of normal ranges of clinical lab parameters for laboratory animals.
- 3). At G.D. Searle: statistical analyses of pre-clinical teratology studies (using SAS and BMDP) and preparation of statistical reports. At Baxter Travenol: Statistical analyses and reports provided for a couple of pre-clinical studies.

(Continued)

EXPERIENCE (CON'T)**SUMMER 1982**

Statistical consultant at Abbott Laboratories, Hospital Products Division, Abbott Park, Ill. Statistical analyses of data and preparation of statistical reports for clinical trials involving mainly hospital parenteral nutritional studies.

1976-1982

Part time (15-24 hours per week) as a radio and TV technician at a TV repair shop in Kirkland, Ill., during graduate school. 1976-1979: Summer positions at William's Electronics and Perkin-Elmer, Corp. as an electronic technician. Contract technician at Motorola and Zenith (cumulative 5 months). About three years cumulative experience as an electronic technician.

CONTINUING EDUCATION

2004 Bruker Optics NIR Training Class.

2000 (Bristol Myers Squibb) Kinetics for Synthetic Chemists by D. Collum, Cornell Univ.

Took following 1-2 day courses at ASA annual meetings:

1993 (San Francisco, Ca.): Confidence Intervals on Variance Components

1992 (Boston, Ma.): Statistical (Confidence) Intervals.

1991 (Atlanta, Ga.): Product/Process Optimization and Variation Reduction.

1991 (Washington, D.C.): Training Course in Nonclinical Statistics (3 days).

1989 (Washington, D.C.): Nonlinear Regression

1988 (New Orleans): Response Surface Methodology.

1986 (Chicago): Density Estimation.

PUBLICATIONS

Sandell Dennis , Vukovinsky Kim , Diener Myron , Hofer Jeff , Pazdan James , Timmermans Joep (2006) Development of a content uniformity test suitable for large sample sizes. Drug Information Journal. 40, 337-344.

Victor W. Rosso, James L. Pazdan, and John J. Venit (2001) Rapid Optimization of the Hydrolysis of N'-Trifluoroacetyl-S-tert-leucine-N-methylamide Using High-Throughput Chemical Development Techniques Org. Proc. Res. Dev., 5 (3), 294 -298

Thomas S. Graves, James L. Pazdan (1995). A Permutation Test Analogue to Tarone's Test for Trend in Survival Analysis, Journal Statistical Computation and Simulation **53**, 79-89.

RECENT PRESENTATIONS

2006, 2005 Pharmaceutical Inspectorate Training Course (for FDA Inspectors and Reviewers), Rockville, MD. How DOE Applies to Pharmaceutical Dosage Forms - Industry's Current Practices for Solid Oral Dosage Forms. Was awarded Certificate of Achievement for Outstanding Contribution for each year.

2005 28th Annual Midwest Biopharmaceutical Statistics Workshop, Muncie, Ind. Statistical Aspects in the Development of NIR Assays.

2003 American Statistical Association National Meeting San Francisco, Ca.

Improved Analysis of Independent 1 Df Mean Squares in Unreplicated 2-Level Factorial Designs Without the Use of Experimental Error.

References Upon Request.

March 9, 2007

DAVID LeBLOND

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GPRD Starting Date: 10-1-97
Dept. # 436 Location: AP9A/1

PRINCIPAL RESEARCH STATISTICIAN

Education:	2005	MS	Statistics	Colorado State University
	1981	Ph.D	Biochemistry	Michigan State University
	1974	MS	Dairy Science	University of Illinois
	1971	BS	Chemistry	University of Illinois
	1967	HS		Mundelein High School
Experience:	1997-Present		Principal Research Statistician	
	<i>GPRD/436</i>			Pharmaceutical and analytical processes. Process and Methods optimization and validation. Stability analyses. Sampling plan development. Application of Bayesian Methods in CMC.
	1995-1997		Statistician	
	<i>ADD/86H</i>			Rare Reagents Process Control. Design and analysis of test method and process validations in manufacturing. Financial optimization of cell culture process.
	1993-1995		Senior Statistician	
	<i>ADD/</i>			Probe Diagnostic Business Unit. Study, design and analysis; clinical data management and preparation of graphics and reports for 3 new gene probe diagnostic products. FDA 510 (k) submissions. Management of SAS local area network system. Support to QC organization.
	1992-1993		Researcher	
				Technician in Muscle Biochemistry research at the University of Illinois, Department of Animal Science.
	1991-1993		Statistical Consultant and Trainer	
	<i>ADD/</i>			Diagnostics R&D Staff. Development of agenda, presentation materials, course booklet and computer exercises. Training of 300+ scientists and engineers. (Video tape available in Abbott Library.) Design and analysis of process characterization and improvement studies. Pre-clinical statistical support. Technical service award in 1993.
	1989-1991		Senior Research Scientist	
	<i>ADD/</i>			Divisional R&D. Optimization of agglutination assay technology. Development of imaging system and data reduction for QC testing. Analysis of research clinical trials.

March 9, 2007

1987-1989

ADD/

Senior Systems Analyst

Divisional R&D. Writing and validation of software design specifications for new diagnostic instrumentation. Development of algorithms for image analysis and assay data reduction. Outstanding performance evaluation. Promotion to senior scientist.

1981-1987

ADD/

Biostatistician

Department of Biometrics, Divisional R&D. Pre-clinical and clinical statistical support. Writing of FORTRAN response surface analysis package. Experimental design course to 200+ Abbott scientists and engineers. \$1,000 service award.

1979-1981

ADD/

Biochemist

Physiology Diagnostics Venture. Kinetic modeling and optimization of enzymatic assay technology.

AFFILIATIONS:

American Statistical Association

13 Professional Publications in various areas of Statistics, Biochemistry and Clinical Chemistry (list available upon request)

13 Abbott technical exchange posters.

YIJIE DONG

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EDUCATION

Ph.D., Pharmaceutical Science, January 2003

Graduate School, Rutgers University, New Brunswick, NJ

M.S., Statistics, January 2000

Graduate School, Rutgers University, New Brunswick, NJ

M.S., Microbiological Pharmacology, June 1996

Institute of Medicinal Biotechnology

Peking Union Medical School (Chinese Academy of Medical Science), Beijing, China

B.S., Microbiology, June 1993

Shandong University, Jinan, China

ACADEMIC HONORS

Research Fellow, Department of Pharmaceutical Science, Rutgers University, 2000-2002

Fellow, New Jersey Quality Control Association, 1999-2000

Recipient, Rutgers University Teaching Assistantship, 1997-1999

Recipient, CUNY (City University of New York) Scientific Fellowship, 1996-1997

Recipient, Shandong University Scholarship, 1989-1993

EXPERIENCE

February, 2005- **Manager Quality Statistics**, Bristol-Myers Squibb Company, New Brunswick, New Jersey

July, 2002-February, 2005 **Senior Statistician**, Bristol-Myers Squibb Company, New Brunswick, New Jersey

- Support quality control and quality assurance of pharmaceutical manufacture on a worldwide basis by providing study design, statistical analysis and consulting.

August 1999-June, 2002 **Research Fellow**, Department of Pharmaceutical Science, Rutgers University, New Brunswick, NJ

- Ph.D. Research – Integration of electrochemically-induced oxidation and competitive kinetic model as an evaluation method for low molecular weight antioxidants

Sept. 1997-July 1999 **Graduate Student**, Department of Pharmaceutical Science, Rutgers University, New Brunswick, NJ

- Analysis of steroids as constituents or contaminants in pharmaceutical products

Sept. 1998-Dec. 1999 **Graduate Student**, Department of Statistics, Rutgers University, New Brunswick, NJ

- Designed statistical sections of clinical trial protocols

- Performed survival analysis and utilized quality control concepts on large real-life data set
- Developed statistical programs and database for statistical analysis and data displays

Sept. 1997-May 1999 **Teaching Assistant**, College of Pharmacy, Rutgers University, New Brunswick, NJ

- Assisted with all aspects of classroom and laboratory teaching of a 200-people class

Sept. 1993-June 1996 **Research Assistant**, Chinese Academy of Medical Science, Beijing, China

- Participated in a major research project sponsored by National Foundation of Natural Sciences of China: "Molecular biology and regulatory mechanisms of secondary metabolic product biosynthesis by *Actinomycetes*".

Mar. 1992-June 1993 **Research Assistant**, National Laboratory of Fermentation, Shandong University

- GC analysis of gas products of liquid-cultured plants

PROFESSIONAL AFFILIATIONS

Member, PhRMA CMC Statistics Expert Team

Member, American Association of Pharmaceutical Scientists

Member, American Statistical Association

COMPETENCIES

Pharmaceutical Analysis, Applied Statistics, Microbiology and Biochemistry

SKILLS

Pharmaceutical Analysis Skills: HPLC, LC-MS, GC, GC/MS, immunoassays, and TLC.

Statistics Software: SAS (Statistical Analysis System), Splus, and R

Computer Skills: Unix, DOS, Windows, Database, Microsoft applications

Others: Knowledge of pharmaceutical regulatory requirements, such as USP, cGMP, and cGLP.

PAPERS and PUBLICATIONS

Y. Dong. Use of electrochemically-induced oxidation as an evaluation method for low molecular weight antioxidants.

Ph. D. Dissertation – Rutgers University, New Brunswick, New Jersey, USA, 2003

L. C. Bailey, T. Medwick, and Y. Dong. Steroid Analysis. *Encyclopedia of Analytical Chemistry*, John Wiley and Sons Ltd., Chichester, 2000

Y. Dong. The pathway and regulation of thienamycin biosynthesis.

Master' Thesis - Institute of Medicinal Biotechnology

Chinese Academy of Medical Science, Beijing, China, 1996