Overview of Designed Experiments

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Overview of Designed Experiments

Objectives

- Understand the strategy of designed experiments.
- Recognize the types of experiments available in Minitab.

Overview

Purpose

This course introduces the concept of full and fractional factorial designed experiments. Using examples, you will learn about design planning, execution, and analysis of designed experiments to identify optimal settings for a process.

Designed experiments consist of series of runs, or tests, in which (1) input variables of a process are simultaneously changed, and (2) responses are observed.

Using this approach for improving a process is much more efficient than other methods, such as "one-factor-at-a-time" experimentation. With designed experiments, in far fewer tests, many factors can be studied simultaneously, while providing independent estimates of factor effects, plus valuable information about factor interactions. Without properly designed experiments, the effects of these interactions are often overlooked.

Applications of designed experiments

Use designed experiments to:

- Determine which factors have a significant effect on a response
- Identify the effect of an interaction between two variables
- Optimize process performance
- Reduce development time for new products
- Reduce variation in a process
- Determine optimal settings of factors that optimize all responses, including safety and cost

Guidelines for using designed experiments

Although designed experiments have a wide range of applications, consider these general guidelines:

1. State the problem under consideration and define the objectives of the study.
2. Choose the factors or input variables to be studied and determine reasonable ranges for each.
3. Determine appropriate responses and how to measure them.
4. Determine the appropriate experimental design.
5. Execute the design.
6. Statistically analyze the resulting data.
7. Verify results using confirmatory runs.
8. Make recommendations.

Successful experimental designs incorporate both process knowledge and sound statistical procedures. Process knowledge is invaluable in the design stages, as well as in the interpretation of results.

Keep in mind that experimental design is commonly an iterative approach. Rarely does one run a large, comprehensive design in which final conclusions are made. This course uses a sequential approach that you should consider when you begin a process improvement project.

Experimental designs in Minitab

Design Platform	Design Type	Description	Number of Factors	In Minitab
Screening Designs	Definitive Screening	• Identifies significant main effects, two-factor interactions and in certain cases, quadratic effects • Runs factors at 3 levels	2–48	**Stat** > **DOE** > **Screening**
	Plackett-Burman	• Identifies significant main effects • Runs factors at 2 levels	2–47	**Stat** > **DOE** > **Screening**

Experimental designs in Minitab

Design Platform	Design Type	Description	Number of Factors	In Minitab
Factorial Designs	Full factorial	• Measures responses at all combinations of the factor levels • Runs factors at 2 levels	2–15	**Stat** > **DOE** > **Factorial**
	Fractional factorial	• Measures responses for a subset of the original full design • Runs factors at 2 levels	2–15	**Stat** > **DOE** > **Factorial**
	Split-Plot	• Models up to 3 hard-to-change factors • Runs factors at 2 levels	2–7	**Stat** > **DOE** > **Factorial**
	Plackett-Burman	• Identifies significant main effects • Runs factors at 2 levels	2–47	**Stat** > **DOE** > **Factorial**

Experimental designs in Minitab

Design Platform	Design Type	Description	Number of Factors	In Minitab
Factorial Designs (continued)	General full factorial	• Measures responses at all combinations of the factor levels • Runs factors at 2 to 100 levels	2–15	**Stat** > **DOE** > **Factorial**
Response Surface Designs	Central composite	• Models curvature in the design space • Often employed after a “vital few” factors have been identified • Used in sequential experimentation	2–10	**Stat** > **DOE** > **Response**
	Box-Behnken	• Models curvature in the design space • Often employed after a “vital few” factors have been identified • Used in nonsequential experimentation	3–7 or 9–10	**Stat** > **DOE** > **Response**

Experimental designs in Minitab

Design Platform	Design Type	Description	Number of Factors	In Minitab
Mixture Designs (designs in which the factors are components of a mixture)	Simplex centroid	• Arranges points in a uniform manner over an L-simplex • Factors are components in a mixture	2–10	**Stat** > **DOE** > **Mixture**
	Simplex lattice	• Similar to centroid designs • Arranges points in a uniform manner, but accommodates more factors • Requires an unconstrained design space	2–20	**Stat** > **DOE** > **Mixture**
	Extreme vertices	• Most commonly used mixture design • Used with constrained design spaces	2–10	**Stat** > **DOE** > **Mixture**
Taguchi Designs	2–5 level designs and mixed levels	• Robust designs • Used to minimize variation and reduce sensitivity to noise factors	Up to 31, depending on the number of levels	**Stat** > **DOE** > **Taguchi**

Introduction to Factorial Designs

Full Factorial Designs

Example 1: Solid Oral Dosage Tablet

Problem

Acetriptan (20 mg) is an immediate release (IR) tablet indicated for the relief of moderate to severe physiological symptoms. The goal of this experiment is to find the particle size and the filler percent (microcrystalline cellulose) to minimize uniformity (relative standard deviation < 5%).

Data collection

The tablet manufacturing settings were fixed at a treatment combination according to the DOE randomization and a batch of product was produced. Ten tablets from each batch were tested for Content Uniformity RSD%. The results from each batch were averaged since these values represent repeats as opposed to replicates.

Tools

- **Create Factorial Design**
- **Descriptive Statistics**
- **Analyze Factorial Design**
- **Factorial Plots**

Data set

OralTablet.MTW

Variable	Description
Particle Size	90th percentile of the particle size distribution (10, 30 microns)
MCC%	Percentage of microcrystalline cellulose in the filler (33.3, 66.7%)
Content Uniformity RSD%	Average tablet content uniformity (relative standard deviation)

Minitab stores the design variables in the following columns: StdOrder, RunOrder, CenterPt, and Blocks.

OralTabletComplete.MTW may also be used.

Factorial designs

What are factorial designs

Factorial designs allow you to simultaneously study the effects of several factors on a process. Varying the levels of the factors simultaneously rather than individually:

- Saves time and expense
- Reveals the interactions between the factors

When to use factorial designs

Use factorial designs to:

- Efficiently estimate the effect of each factor on the response
- Estimate the effects of interactions between two or more factors on the response
- Test for curvature in the response by including center points in the design

Why use factorial designs

Use factorial designs to answer questions such as:

- Which variables most strongly influence the response?
- What factor settings optimize the response?

For example,

- How do metal hardness, cutting speed, and cutting angle affect the life of a metal cutting tool?
- What settings of sweetener, syrup-to-water ratio, carbonation level, and temperature maximize the taste scores of a new soft drink?

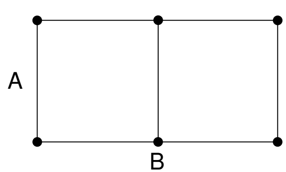
Full factorial designs

What are full factorial designs

A full factorial experiment measures all combinations of the experimental factor levels. The combinations of factor levels represent the experimental conditions at which responses are measured. Each experimental condition is a *run* and each response measurement is an *observation*. The entire set of runs is the *design*.

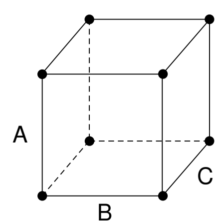
The following diagrams show two- and three-factor designs. Each point represents a unique combination of factor levels. For example, in the two-factor design, the point on the lower left corner represents the experimental run when Factor A is set at its low level and Factor B is also set at its low level.

Two factors



Two levels of Factor A Three levels of Factor B

Three factors



Two levels of each factor

When to use full factorial designs

Minitab provides two types of full factorial designs:

- Use a two-level factorial design (2^k design) when each experimental factor has only two levels.
- Use a general full factorial design when any experimental factor has more than two levels. For example, Factor A may have two levels, Factor B may have three levels, and Factor C may have five levels.

Why use full factorial designs

Use factorial designs to answer questions such as:

- Which variables most strongly influence the response?
- Do interactions between two or more factors influence the response?
- What factor settings optimize the response?

For example,

- How do glass type and phosphor type affect the brightness of a television tube?
- How does the interaction between temperature and sugar affect chocolate smoothness?
- Which nozzle shape on a water-jet cutting tool minimizes the time needed to cut a standard metal sheet?

Full factorial designs

Creating a factorial design

With 2 factors, the only design option is a full factorial design, which requires 4 runs, 1 for each treatment combination. Replicating this design 4 times results in 16 runs.

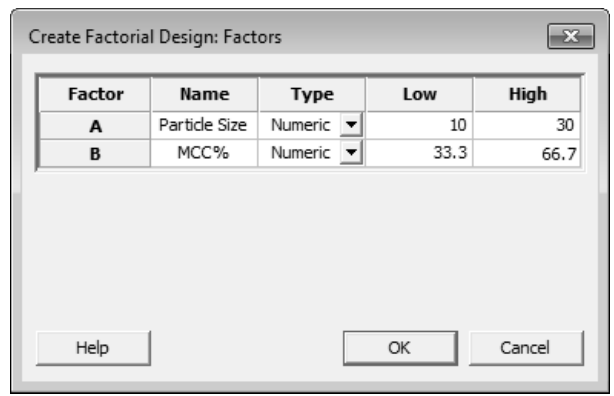
Factor levels

By default, Minitab names factors alphabetically and codes settings as follows: low = –1, high = +1. In the **Factors** sub-dialog box, you can specify the actual factor names and settings.

Minitab displays the model coefficients for response variables in coded and uncoded units.

Create Factorial Design

1. Choose **Stat** > **DOE** > **Factorial** > **Create Factorial Design**
2. Click **Designs**.
3. From **Number of replicates for corner points**, choose **4**, then click **OK**.
4. Click **Factors**.
5. Complete the dialog box as shown below.



6. Click **OK** in each dialog box.

Interpreting your results

Each column in the design is identified by its name.

The worksheet contains a column for each factor and columns containing design information that Minitab requires to conduct the analysis. Although you can change values within a column, you cannot move columns without corrupting the design.

If you corrupt a design, go to **Define Custom Factorial Design** and redefine the columns.

Changing display order

You can display the design in either run order (default) or standard order. Run order is random; use it when you conduct the experiment. The standard order view makes the generated design easier to understand.

Displaying factor levels

Display factor levels as actual values or in coded units. When displayed in coded units, the values are coded as low and high levels (–1, 1).

What's next

Use **Display Design** to view the design in Yates' (standard) order and coded units.

↓	C1	C2	C3	C4	C5	C6
	StdOrder	RunOrder	CenterPt	Blocks	Particle Size	MCC%
1	15	1	1	1	10	66.7
2	7	2	1	1	10	66.7
3	11	3	1	1	10	66.7
4	4	4	1	1	30	66.7
5	3	5	1	1	10	66.7
6	9	6	1	1	10	33.3
7	1	7	1	1	10	33.3
8	14	8	1	1	30	33.3
9	2	9	1	1	30	33.3
10	12	10	1	1	30	66.7
11	13	11	1	1	10	33.3
12	5	12	1	1	10	33.3
13	16	13	1	1	30	66.7
14	10	14	1	1	30	33.3
15	8	15	1	1	30	66.7
16	6	16	1	1	30	33.3

Note Minitab uses a random number generator to determine the run order. Although your run order will not match the run order shown here, the standard order will match.

Checking orthogonality

To evaluate the orthogonality of a design, change the worksheet display to coded units. The design may be easier to understand in standard order.

Advantages of an orthogonal design

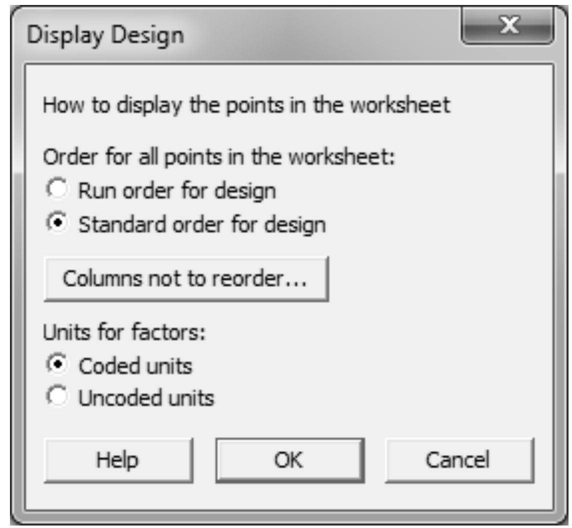
- Model terms (effects and interactions) are estimated independently.
- Analysis is simpler because effects are independent of one another. When reducing a model, you can simultaneously remove all terms that are not significant.

Minitab and orthogonal designs

Using **Create Factorial Design**, Minitab generates an orthogonal design by default. When a design is analyzed in uncoded units, it may no longer be orthogonal. For this reason, Minitab always uses coded units to perform the analysis.

Display Design

1. Choose **Stat** > **DOE** > **Display Design**.
2. Complete the dialog box as shown below.



3. Click **OK**.

Interpreting your results

Orthogonality

When the factors in a design are orthogonal, you can estimate the effects of each factor independently.

If two factor columns are orthogonal, the following conditions hold:

- The sum of each column is zero.
- The correlation between the two columns is zero.

Standard order

The standard order for the two factors, Particle Size and MCC%, is shown in the worksheet on the right. The Particle Size column alternates between –1 and +1; the MCC% column alternates between two –1s followed by two +1s.

Replicates

Replicating an experiment means that each factor combination is run more than one time. This example includes four replicates. The first four rows represent a single replicate of the experiment, with one treatment per row. This pattern continues three more times for a total of four replicates.

↓	C1	C2	C3	C4	C5	C6
	StdOrder	RunOrder	CenterPt	Blocks	Particle Size	MCC%
1	1	7	1	1	-1	-1
2	2	9	1	1	1	-1
3	3	5	1	1	-1	1
4	4	4	1	1	1	1
5	5	12	1	1	-1	-1
6	6	16	1	1	1	-1
7	7	2	1	1	-1	1
8	8	15	1	1	1	1
9	9	6	1	1	-1	-1
10	10	14	1	1	1	-1
11	11	3	1	1	-1	1
12	12	10	1	1	1	1
13	13	11	1	1	-1	-1
14	14	8	1	1	1	-1
15	15	1	1	1	-1	1
16	16	13	1	1	1	1

Adding response data

The response variable is the average Content Uniformity RSD%. Add the measurement (response) to the worksheet by typing the data into a new column.

Before entering the data shown at right, make sure your design is displayed in standard order. This ensures the data is entered in the proper rows.

Data window

1. Press **Ctrl+D** to move to the **Data** window.
2. Name column C7 *Content Uniformity RSD%*.
3. Type the following values in rows 1–16 of Content Uniformity RSD% (C7): *4.1*, *2.9*, *5.0*, *3.8*, *4.0*, *3.1*, *5.1*, *4.0*, *3.9*, *3.1*, *5.4*, *3.9*, *4.2*, *3.2*, *5.1*, *4.1*

Displaying your design

Displaying coded versus uncoded units

Display Design shows the data in coded or uncoded units while in standard or run order.

Minitab always analyzes the data in coded units, regardless of the design display.

What’s next

Display a summary table to investigate the average adhesion at each treatment combination.

Display Design

1. Choose **Stat** > **DOE** > **Display Design**.
2. Under **Units for factors**, choose **Uncoded units**.
3. Click **OK**.

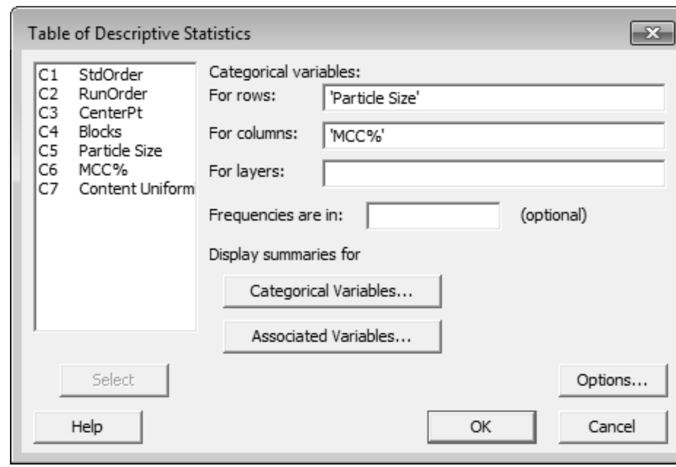
Defining factor effects

Before interpreting the analysis results, you need to understand the factor effects.

Display a summary table containing the average Content Uniformity RSD% for each combination of Particle Size and MCC%, as well as the overall average Content Uniformity RSD% for each Particle Size level and each MCC%.

Descriptive Statistics

1. If you did not enter the response data, open the file OralTablet.MTW.
2. Choose **Stat** > **Tables** > **Descriptive Statistics**.
3. Complete the dialog box as shown below.



Defining factor effects

You can use average uniformity values to calculate the main effects for each factor.

Descriptive Statistics (continued)

4. Click **Associated Variables**. In **Associated variables**, enter *'Content Uniformity RSD%'*.
5. Under **Display**, check **Means**.
6. Click **OK** in each dialog box.

Interpreting your results

Main effects

Use the table of the means to understand a factor effect. An effect is the difference between the average response at the high (+1) and low (–1) levels of a factor.

Main effects are calculated using the means in the All column and All row.

- The main effect for Particle Size is the mean response at Particle Size 30 minus the mean response at Particle Size 10:
  3.512 – 4.600 = –1.088

  On average, the uniformity is 1.088 less with the higher particle size.

- The main effect for MCC% is the mean response at MCC% 66.7 minus the mean response at MCC% 33.3:
  4.550 – 3.563 = 0.987

  On average, the uniformity is 0.987 more with the higher MCC%.

Rows: Particle Size   Columns: MCC%

	33.3	66.7	All
10	4.050	5.150	4.600
	4	4	8
30	3.075	3.950	3.512
	4	4	8
All	3.563	4.550	4.056
	8	8	16

Cell Contents
Content Uniformity RSD% : Mean
Count

Interpreting your results

Interaction effects

Interaction effects are calculated from the means within each treatment. Here, the interaction effects are calculated using these means:

- 4.050 for 10 and 33.3
- 5.150 for 10 and 66.7
- 3.075 for 30 and 33.3
- 3.950 for 30 and 66.7

The interaction effect between Particle Size and MCC% is:

(10:33.3 + 30:66.7)/2 – (10:66.7 + 30:33.3)/2

= (4.050+3.950)/2 – (5.150+3.075)/2

= –0.1125

Rows: Particle Size Columns: MCC%

	33.3	66.7	All
10	4.050	5.150	4.600
	4	4	8
30	3.075	3.950	3.512
	4	4	8
All	3.563	4.550	4.056
	8	8	16

Cell Contents
Content Uniformity RSD% : Mean
Count

What's next

Analyze the experimental data using these two steps:

1. Fit several models to find one that represents the data.
2. Use factorial plots to visualize main effects and interactions and to find the best factor settings.

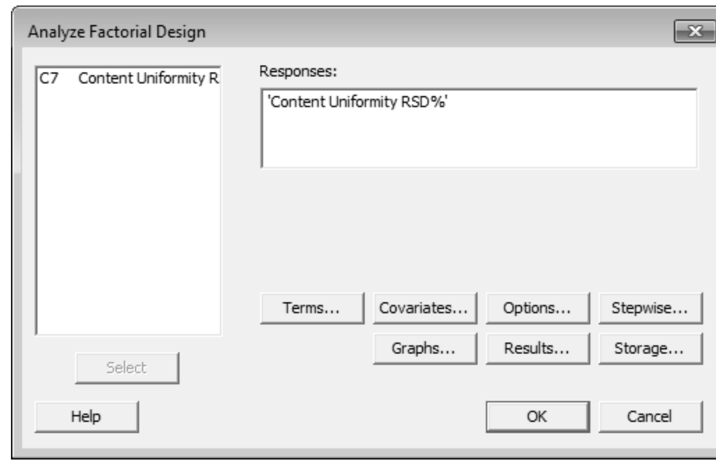
Fitting the model

If you enter more than one response, Minitab performs a separate analysis for each one.

After choosing the response, click **Terms** to select the model.

Analyze Factorial Design

1. Choose **Stat** > **DOE** > **Factorial** > **Analyze Factorial Design**.
2. Complete the dialog box as shown below.



Fitting the model

By default, Minitab includes the maximum number of terms possible in the model. These terms are shown in the **Selected Terms** list. You can analyze the model chosen by Minitab or specify a different model.

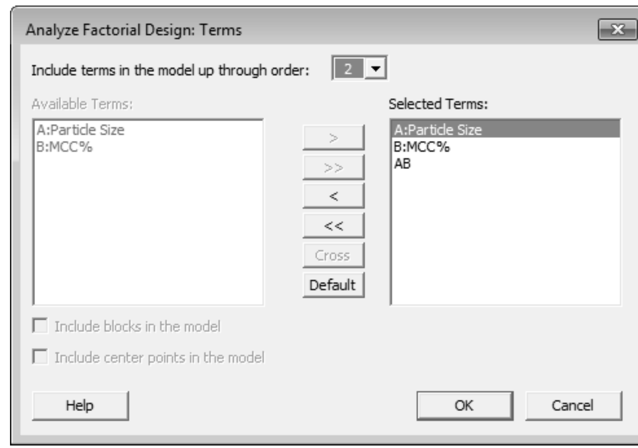
Selecting terms

You can select model terms in two ways:

- Move desired terms from the **Available Terms** list to the **Selected Terms** list using the arrows or by double-clicking each term.
- Specify terms by order. For example, include terms through order 3 to enter main effects, two-way interactions, and three-way interactions in the model.

Analyze Factorial Design (continued)

3. Click **Terms**.
4. Verify the dialog box appears as shown below.



5. Click **OK**.

Fitting the model

To determine whether any terms placed in the model have significant effects, use the following:

- P-values displayed in the effects table
- Pareto chart of the effects

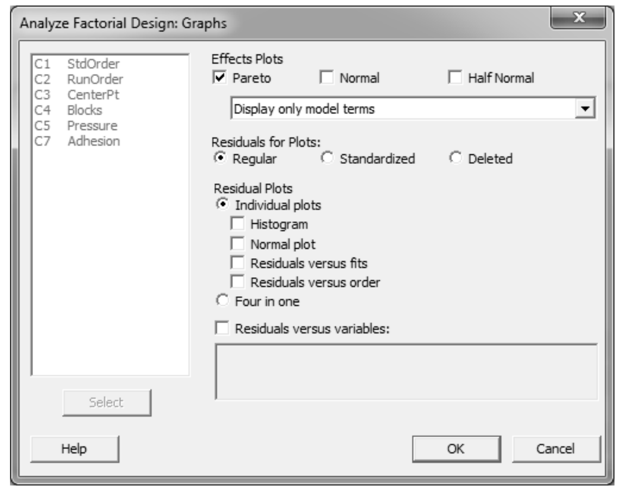
Alpha (α)

In a 2^k design, α is the risk of incorrectly concluding that a factor has a significant effect.

Choose an α-level appropriate for the objectives of the experiment. When making final process decisions from a factorial DOE, a low α-level may be appropriate (for example, 0.05). Factorial designs can screen many factors and help to identify which are important for further experimentation. In screening applications, you might choose a higher α-level (for example, 0.10).

Analyze Factorial Design (continued)

6. Click **Graphs**.
7. Verify that the dialog is as shown below.



8. Click **OK** in each dialog box.

Interpreting your results

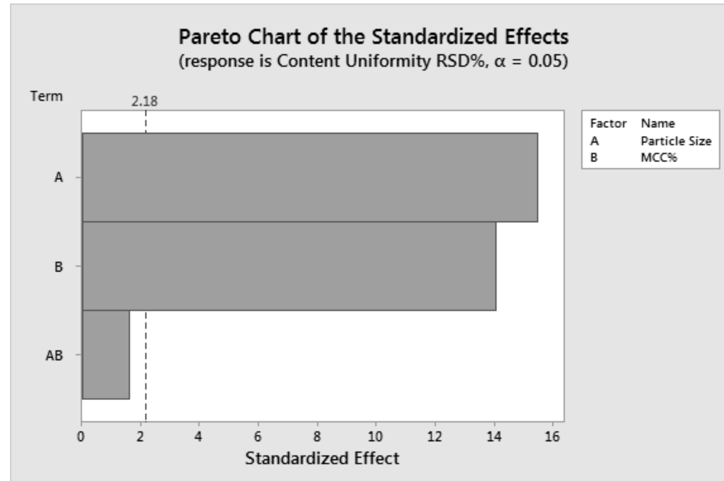
A Pareto chart of effects shows which terms contribute the most to the variability in the response. Here, the chart shows which factors significantly affect adhesion and the relative magnitude of each effect.

This plot displays the following:

- The terms from top to bottom in decreasing order of importance.
- A reference line at the α = 0.05 significance level; any bar extending beyond the line is a significant effect.

The Pareto chart shows that both Particle Size and MCC% significantly affect uniformity. The interaction between the terms (AB) is not significant.

Although the Pareto charts shows the magnitude of an effect, it does not indicate the direction of the effect.



Interpreting your results

The effects previously calculated using the table of means are listed in the coefficients table. The effects are:

- –1.0875 for Particle Size
- 0.9875 for MCC%
- –0.1125 for the Particle Size-by-MCC% interaction

Use the p-values in the coefficients table to determine which terms are statistically significant at the α = 0.05 level:

- Particle Size and MCC% are significant (P-Value = 0.000 and P-Value = 0.000).
- The interaction effect is not significant (P-Value = 0.136).

What's next

Exclude the interaction term and refit the model.

Coded Coefficients

Term	Effect	Coef	SE Coef	T-Value	P-Value	VIF
Constant		4.0563	0.0352	115.33	0.000	
Particle Size	-1.0875	-0.5438	0.0352	-15.46	0.000	1.00
MCC%	0.9875	0.4938	0.0352	14.04	0.000	1.00
Particle Size*MCC%	-0.1125	-0.0563	0.0352	-1.60	0.136	1.00

Model Summary

S	R-sq	R-sq(adj)	R-sq(pred)
0.140683	97.34%	96.67%	95.27%

Analysis of Variance

Source	DF	Adj SS	Adj MS	F-Value	P-Value
Model	3	8.68188	2.89396	146.22	0.000
Linear	2	8.63125	4.31562	218.05	0.000
Particle Size	1	4.73062	4.73062	239.02	0.000
MCC%	1	3.90063	3.90063	197.08	0.000
2-Way Interactions	1	0.05063	0.05063	2.56	0.136
Particle Size*MCC%	1	0.05063	0.05063	2.56	0.136
Error	12	0.23750	0.01979		
Total	15	8.91937			

Reducing the model

To remove the interaction term from the model, do one of the following:

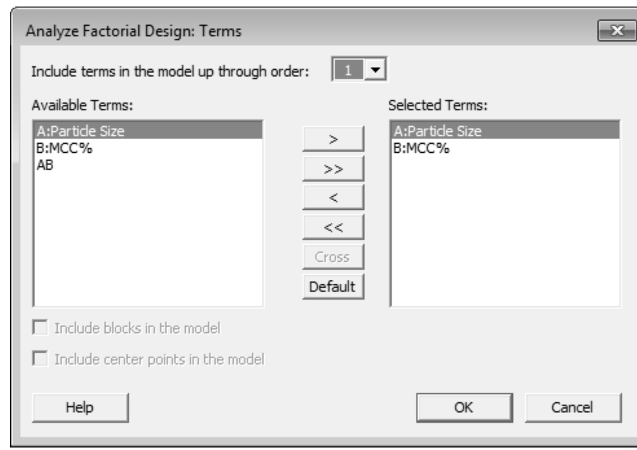
- From **Include terms in the model up through order**, choose **1**.
- Highlight **AB** in the **Selected Terms** box and click < .
- Double-click **AB** in the **Selected Terms** box.

Minitab uses the remaining terms (**A** and **B**) to model the response.

The reduced model should remain hierarchical in Minitab. In a hierarchical model, if an interaction term is included, all main effects that comprise the interaction term are also in the model.

Analyze Factorial Design

1. Choose **Stat** > **DOE** > **Factorial** > **Analyze Factorial Design** or press **Ctrl+E**.
2. Click **Terms**.
3. Complete the dialog box as shown below.



4. Click **OK**.

Verifying model assumptions

To confirm that the analysis is valid, verify all assumptions about the model error term. Use residual plots to check that the errors have the following characteristics:

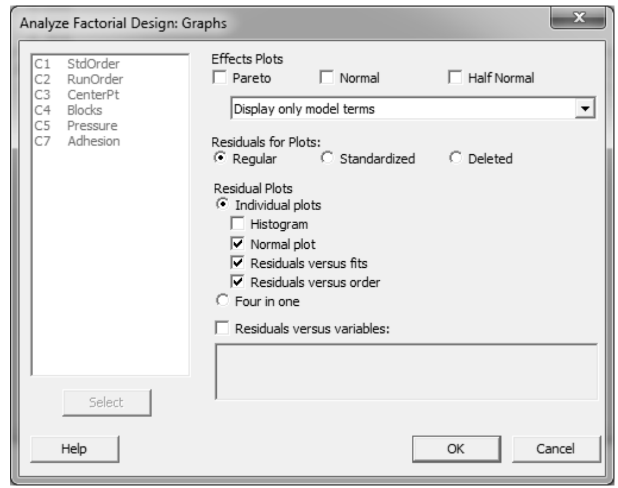
- Normally distributed
- Constant variance for all fitted values
- Random over time

Note In DOE, you often start with a full model and remove terms that are not significant. If you remove very few terms from the full model the residuals may be highly structured, making it difficult to use them to check model assumptions.

Analyze Factorial Design (continued)

5. Click **Graphs**.

6. Complete the dialog box as shown below.



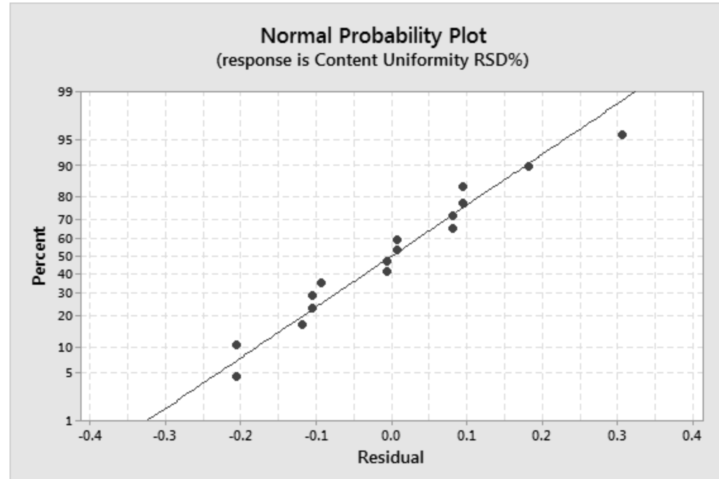
7. Click **OK** in each dialog box.

Interpreting your results

Normal probability plot

The normal probability plot should roughly follow a straight line. Use this plot to verify that the residuals do not deviate substantially from a normal distribution.

This pattern...	Indicates...
Not a straight line	Residuals are not from a normal distribution
Curved (residuals are from a skewed distribution)	Heavy or light tails in the distribution
Points far away from the line	Outliers exists
Changing slope	A variable may be missing from the model



For the uniformity data, the normal probability plot shows that the residuals generally follow a straight line. Assume that the residuals follow a normal distribution.

You can also use the normal probability plot to identify outliers, which are points that lie far from most other points on the plot. For this example, the plot indicates no outliers.

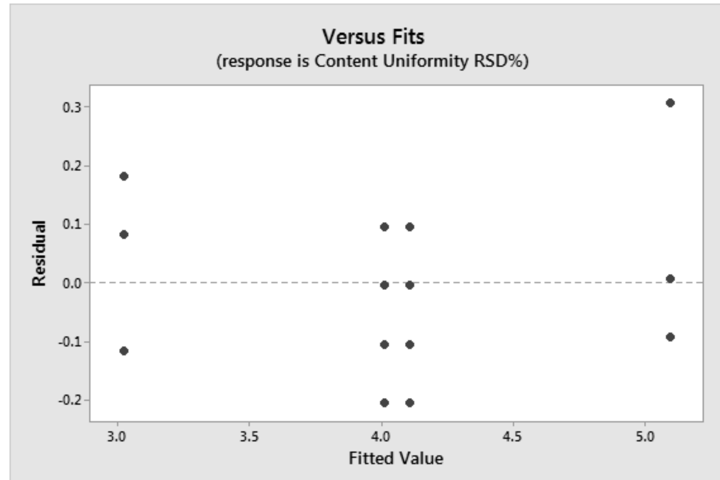
Interpreting your results

Residuals versus fits

Use the plot of the residuals versus fits to verify that the residuals are scattered randomly about zero.

This pattern…	Indicates…
Curvilinear	A quadratic term may be missing from the model
Fanning or uneven spread of residuals across the different fitted values	Nonconstant variance of the residuals
Points far away from zero relative to other data points	Outliers exist

For the uniformity data, the residuals versus the fitted values plot shows a random spread, which indicates a constant variance of the residuals. The plot also indicates no major outliers.



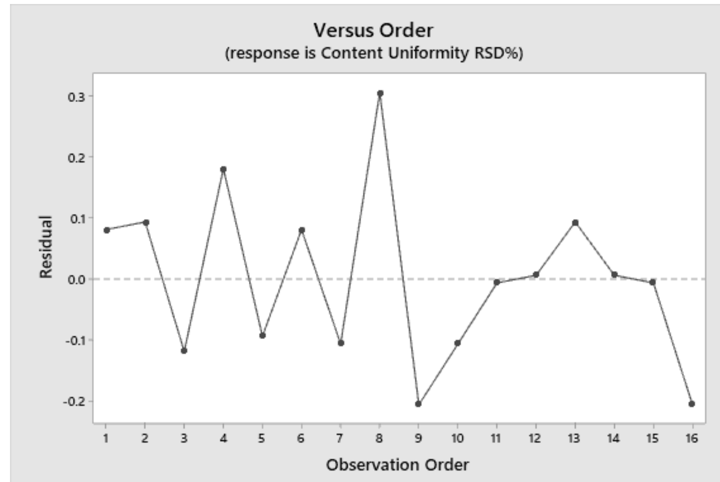
Interpreting your results

Residuals versus order

The plot of the residuals versus order displays the residuals in the order of data collection (provided the data were entered in the same order in which they were collected). If the data collection order affects the results, residuals near each other may be correlated, and thus, not independent.

This pattern...	Indicates...
Residuals are not randomly scattered around zero	Residuals are not independent over time
Residuals are randomly scattered around zero	Residuals are independent
Points far away from zero	Outliers exist

For the uniformity data, the residuals seem randomly scattered around zero.



Interpreting your results

The low p-values (0.000 and 0.000) for both factors indicate that Particle Size and MCC% significantly affect uniformity.

Notice that:

- The Particle Size effect is negative (-1.0875), because the uniformity was higher, on average, at the lower Particle Size.
- The MCC% effect is positive (0.9875), because the uniformity was higher, on average, at the higher MCC%.

Coded Coefficients

Term	Effect	Coef	SE Coef	T-Value	P-Value	VIF
Constant		4.0563	0.0372	108.98	0.000	
Particle Size	-1.0875	-0.5438	0.0372	-14.61	0.000	1.00
MCC%	0.9875	0.4937	0.0372	13.27	0.000	1.00

Interpreting your results

S

S is the standard deviation in the model. S is the square root of the Residual Error Adj MS, often called MSE.

R^2, adjusted R^2, and predicted R^2

R^2 is the proportion of the variability in the response explained by the regression equation. Thus, 96.77% of the variation in uniformity can be explained by its relationship with Particle Size and MCC%.

Adjusted R^2 is sensitive to the number of terms in the model and is useful when comparing models with different numbers of terms.

Predicted R^2 reflects how well the model will predict future data.

Lack of fit

The ANOVA table includes a lack-of-fit test. The null hypothesis is that this model fits the response data.

The p-value (0.136) is greater than 0.05, indicating you should not reject the null hypothesis. Rejecting the null hypothesis usually indicates that you have omitted important terms from the model.

Model Summary

S	R-sq	R-sq(adj)	R-sq(pred)
0.148874	96.77%	96.27%	95.11%

Analysis of Variance

Source	DF	Adj SS	Adj MS	F-Value	P-Value
Model	2	8.63125	4.31562	194.72	0.000
Linear	2	8.63125	4.31562	194.72	0.000
Particle Size	1	4.73062	4.73062	213.44	0.000
MCC%	1	3.90062	3.90062	175.99	0.000
Error	13	0.28813	0.02216		
Lack-of-Fit	1	0.05063	0.05063	2.56	0.136
Pure Error	12	0.23750	0.01979		
Total	15	8.91937			

Interpreting your results

Predictive equation

The final model in uncoded units is:

Content Uniformity RSD% = 3.665 – 0.05438 * Particle Size + 0.02957 * MCC%

Note that for text factors, the coefficient in uncoded units is the same as the coefficient in coded units.

Unusual observations

The table of unusual observations indicates that observation 8 is an outlier because its residual is more than 2 standard deviations from the mean of 0. Outliers often occur by chance, but you should check for a potential cause.

What's next

Use factorial plots to find the factor settings that optimize the response.

Regression Equation in Uncoded Units

Content Uniformity RSD% = 3.665 - 0.05438 Particle Size + 0.02957 MCC%

Fits and Diagnostics for Unusual Observations

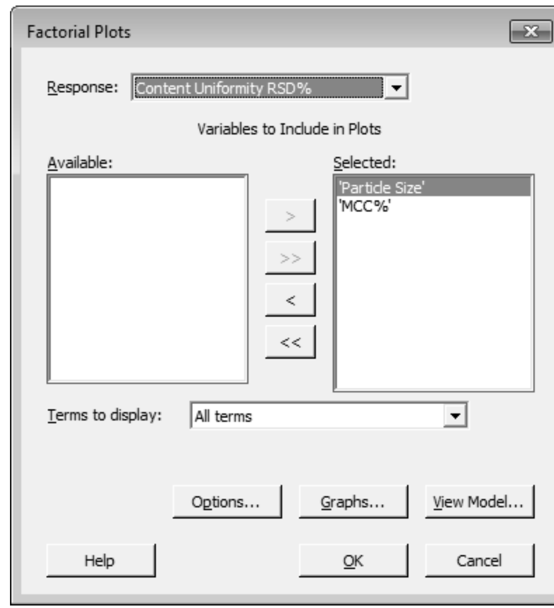
Obs	Content Uniformity RSD%	Fit	Resid	Std Resid	
8	5.4000	5.0938	0.3063	2.28	R

Visualizing the best setting combination

After you choose the appropriate model for the data, use factorial plots to visualize the results.

Factorial Plots

1. Choose **Stat** > **DOE** > **Factorial** > **Factorial Plots**.
2. Complete the dialog box as shown below.



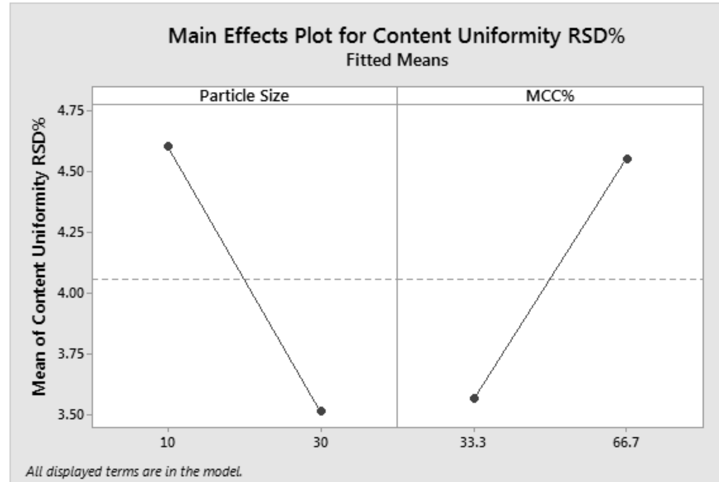
3. Click **OK**.

Interpreting your results

The main effects plot indicates that:

- Larger Particle Size results in smaller content uniformity RSD%
- Lower MCC% results in smaller content uniformity RSD%.

You should confirm that the effects on the plot are statistically significant. In this example, Particle Size and MCC% are significant.

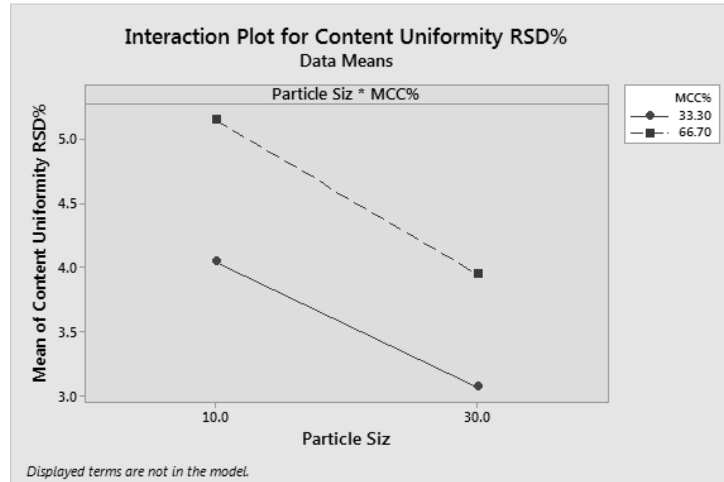


Interpreting your results

The interaction plot shows that, regardless of the MCC%, higher Particle Size results in smaller Content Uniformity RSD%.

The nearly parallel lines suggest there is no interaction between Particle Size and MCC%. The p-value in the statistical analysis (see page 30) indicated that this interaction is not significant.

Note The interaction plot has a gray background because this term is not in the model, as indicated by the footnote.

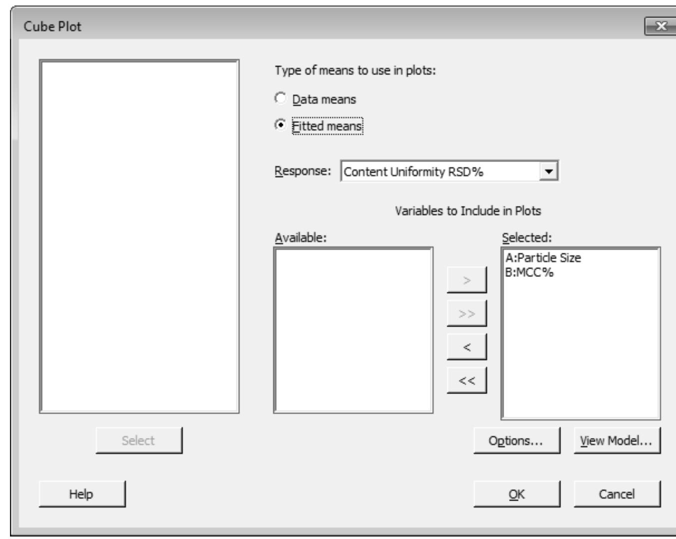


Visualizing the best setting combination

To see the response for each combination of the factor levels, display a cube plot.

Cube Plot

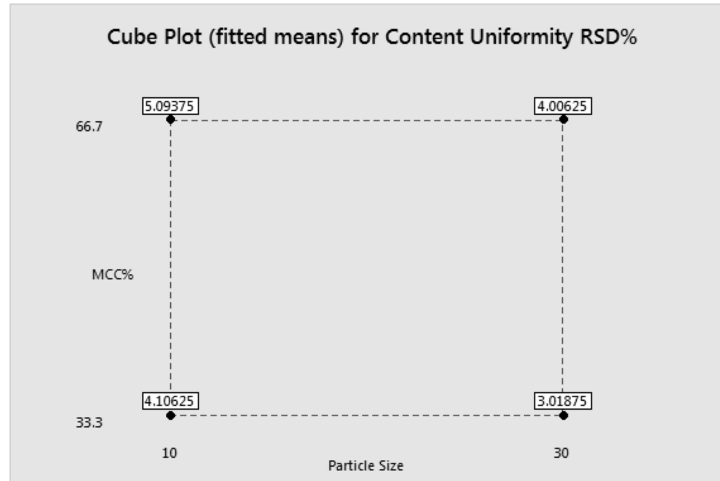
1. Choose **Stat** > **DOE** > **Factorial** > **Cube Plot**.
2. Verify that the dialog box appears as shown below.



3. Click **OK**.

Interpreting your results

Because the design has only two factors, the cube plot is a rectangle. Using the plot, you can easily see the effect of setting levels for both factors simultaneously. The smallest uniformity (3.01875) is expected when a low MCC% is applied with a higher Particle Size.



Final considerations

Summary and conclusions

The experiment indicated that MCC% is minimized when a lower MCC% is applied using a higher Particle Size.

To...	Use...
Identify important terms in the model	A Pareto chart, normal probability plot of effects, or p-values
Obtain information about the constant and blocking terms	The table of coefficients
Consider the effect of simultaneously removing two or more terms	A lack-of-fit test
Evaluate normality, independence, and equal variance of the residuals	Residual plots
Visualize main effects and two-way interactions	Main effects and interaction plots
Show predicted means at all treatment combinations	Cube plots

Additional considerations

The quality team should consider the cost along with the statistical results to ensure that the decreased uniformity is cost justified. They may choose to use less than “optimal” factor settings if the amount of improvement is not enough to justify a substantial increase in production costs.

Response Optimizer

Example 2: Optimizing Solid Oral Dosage Tablet

Problem

The quality team wants to confirm the best settings for Particle Size and MCC% identified using the graphical methods in the previous example. To do this, they use the response optimizer.

Data collection

The tablet manufacturing settings were fixed at a treatment combination according to the DOE randomization and a batch of product was produced. Ten tablets from each batch were tested for Content Uniformity RSD%. The results from each batch were averaged since these values represent repeats as opposed to replicates.

Tools

- **Response Optimizer**

Data set

OralTabletComplete.MTW

Variable	Description
Particle Size	90th percentile of the particle size distribution (10, 30 microns)
MCC%	Percentage of microcrystalline cellulose in the filler (33.3, 66.7%)
Content Uniformity RSD%	Average tablet content uniformity (relative standard deviation)
Minitab stores the design variables in the following columns: StdOrder, RunOrder, CenterPt, and Blocks.	

Response optimizer

What is the response optimizer

Many designed experiments determine optimal factor settings that produce the “best” value for a response of interest. The response optimizer uses the most recent model fit to calculate a solution based on desirability criteria. A response can be minimized, maximized, or aimed at a target value.

Desirability has a range of 0 to 1. A value of 1 represents the ideal case; 0 indicates that one or more responses are outside their acceptable limits. As the response moves away from the target toward the upper or lower bounds (depending on the goal), desirability decreases.

When to use the response optimizer

Use the response optimizer to help identify the combination of input variable settings that optimize a single response or jointly optimize a set of responses. Joint optimization must satisfy the requirements for all the responses in the set. The response optimizer is particularly helpful when many responses are being considered.

Note Although numerical optimization with graphical analysis can provide useful information, it is not a substitute for subject matter expertise. Be sure to use relevant background information, theoretical principles, and knowledge gained through observation or previous experimentation when applying these methods.

Why use the response optimizer

Use the response optimizer to confirm graphical results or to determine the optimal factor settings based on the fitted model.

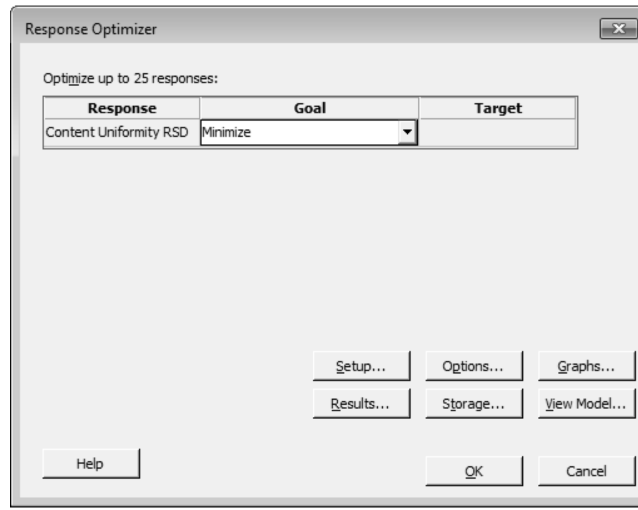
Optimizing the response

Using the model fit from the previous example, apply the response optimizer to determine the best settings for Particle Size and MCC%. Remember that the final model contains only main effects.

In this example, the goal is to minimize uniformity.

Response Optimizer

1. Open OralTabletComplete.MTW.
2. Choose **Stat** > **DOE** > **Factorial** > **Response Optimizer**.
3. Complete the dialog box as shown below.



Optimizing the response

Goal

When using the response optimizer, it is not necessary to specify any values under **Setup**. However, if certain values are desired or there are multiple responses, numbers can be entered for the lower, target, and/or upper to refine the optimization.

They would like the mean content uniformity to be less than 2.5 and the upper acceptable mean content uniformity is 4. As the response moves away from the target in the **Setup** toward the upper or lower bounds (depending on the goal), desirability decreases.

Note that when the goal is changed to minimize, only the target and upper desirability values are required; the lower bound is not.

Weight

In Minitab's approach to optimization, each response is transformed using a specific desirability function. The weight defines the shape of the desirability function for each response. You can select a weight from 0.1 to 10 to emphasize or de-emphasize the importance of hitting the target value:

- A weight < 1 places less emphasis on the target
- A weight = 1 places equal importance on the target and the bounds
- A weight > 1 places more emphasis on the target

Response Optimizer (continued)

4. Click **Setup**.
5. Complete the dialog box as shown below.

Response	Goal	Lower	Target	Upper
Content Uniformity RSD	Minimize	2.5	2.5	4

6. Click **OK** in each dialog box.

Interpreting your results

Desirability

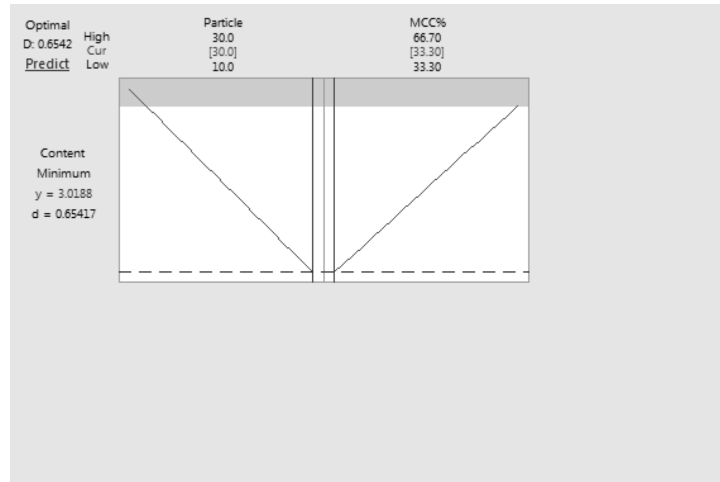
Minitab optimizes the overall desirability of uniformity (D = 0.6542). In this case only one response exists, so the overall desirability is the same as the individual desirability.

The settings needed to achieve the predicted minimum value of Content Uniformity RSD% (3.0188) are:

Particle Size = 30

MCC% = 33.3

If you move the red lines on the graph using the mouse, you can see how changing these settings affects the predicted response.



Note Although Minitab uses the model to find the best predicted response, this result may not be the most practical or cost effective. You should use the response optimizer to see whether more practical factor settings can yield desirable results.

Interpreting your results

Response optimization table

Minitab displays the desirability parameters for each response as well as the factor settings that optimize the response, the predicted response, and the composite desirability.

Confidence interval

The 95% confidence interval defines the likely range of values for the population mean of the response at each factor combination. You are 95% confident that the population mean of all tablets using particle size of 30 with a MCC% of 33.3 will have uniformity between 2.8795 and 3.1580.

Prediction interval

The 95% prediction interval defines the likely range of values for a future observation. You are 95% confident that a future tablet using particle size of 30 with a MCC% of 33.3 will have uniformity between 2.6683 and 3.3692.

Parameters

Response	Goal	Lower	Target	Upper	Weight	Importance
Content Uniformity RSD%	Minimum		2.5	4	1	1

Solution

Solution	Particle Size	MCC%	Content Uniformity RSD% Fit	Composite Desirability
1	30	33.3	3.01875	0.654167

Multiple Response Prediction

Variable	Setting
Particle Size	30
MCC%	33.3

Response	Fit	SE Fit	95% CI	95% PI
Content Uniformity RSD%	3.0188	0.0645	(2.8795, 3.1580)	(2.6683, 3.3692)

Final considerations

Summary and conclusions

- To optimize uniformity, use Particle Size of 30 with a MCC% of 33.3.
- Higher levels of MCC% and lower levels of Particle Size produce acceptable results and may be necessary in production.

Additional considerations

- Because the response optimizer uses the last fitted model for each response, check to make sure the correct terms were in the last model that you fit.
- There is no guarantee that a unique optimum exists. Although the optimizer gives one solution, more than one optimal area may exist.
- The relative importance of each response is subjective. Base importance on your practical and technical knowledge of the process.
- Perform confirmatory runs to validate any conclusions you make based on a designed experiment.