

Case Study: Using Powerful Data Analysis Tools to Ensure Quality Compliance in Pharmaceutical Manufacturing

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Case Study: Powerful Data Analysis Tools in Pharmaceutical Manufacturing

- ▶ A pharmaceutical company has developed a new drug to reduce the level of cytokines (protein) in the blood. Cytokines are associated with a life-threatening medical condition known as sepsis.
- ▶ The drug has been proven safe in adults with doses up to 1500 mg.
- ▶ The initial goal of this study is to determine the daily dose that provides a 20% reduction in cytokines.

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► Stages:

- Use a Gage R&R Crossed to evaluate the measuring system.
- Use Regression to determine the dose needed to get the expected cytokines reduction to 20%.
- Once this has been achieved, the goal is to determine if the drug can be manufactured to meet quality standards.
 - Capability Analysis

Can I trust my data? - Gage R&R

► Example:

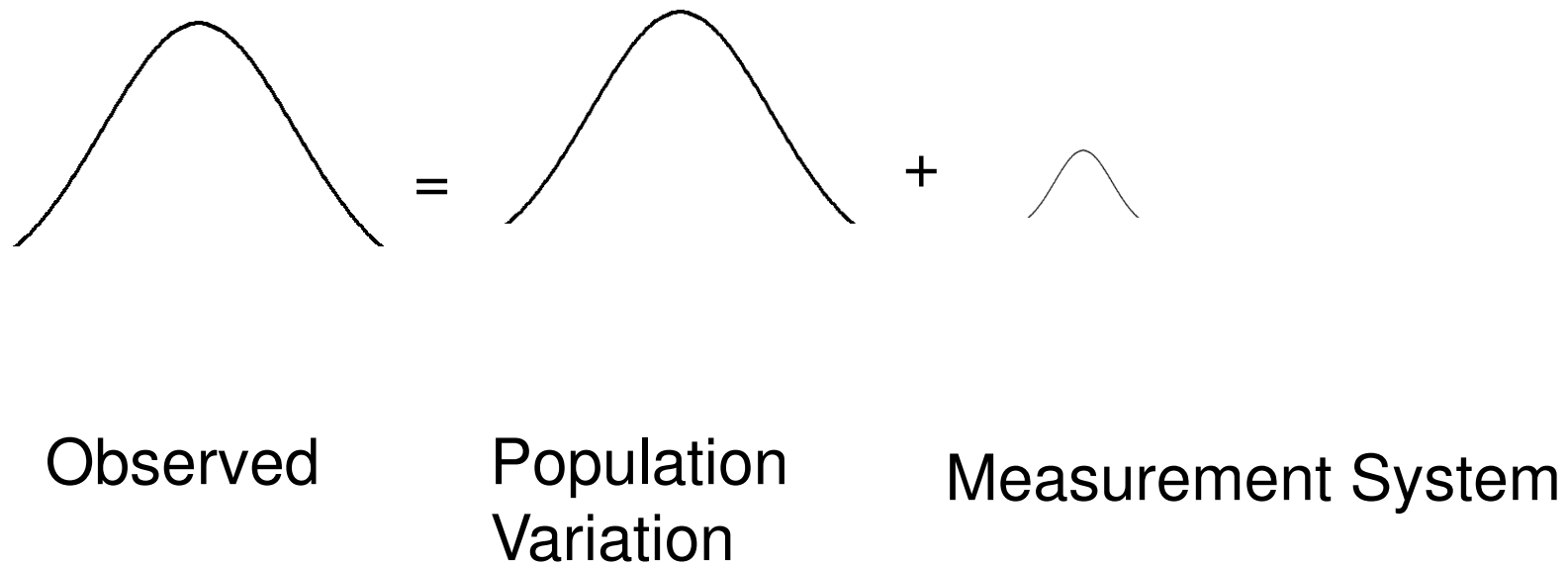
- Use a Gage R&R Crossed to evaluate the measuring system. The number of cytokines per ml is the measurement of interest.
- Researchers randomly selected 10 blood samples and 3 operators. Each of the 10 samples was split into 9 sub-samples.
- Assume that each sub-sample has the same number of cytokines per ml.



Sample	Operators	Cytokines per ml
4	Kellen	275
1	Kellen	227
3	Kellen	276
4	George	277
7	George	256
9	George	259
1	George	227
3	George	272
6	George	246
.....		
3	George	273
7	George	252
10	George	227
5	George	238
9	George	259
3	Bruce	274
5	Bruce	240
4	Bruce	281

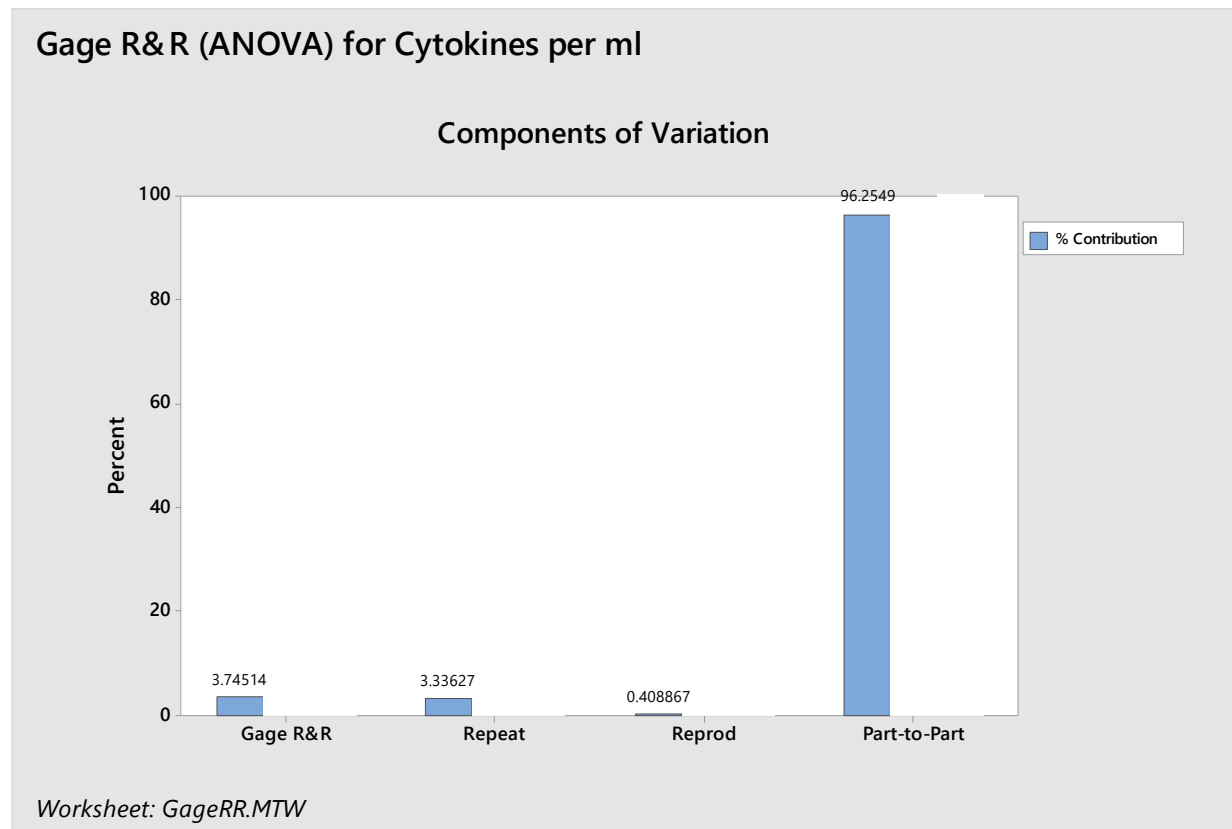
Can I trust my data? - Gage R&R

- ▶ What is a good measurement system?



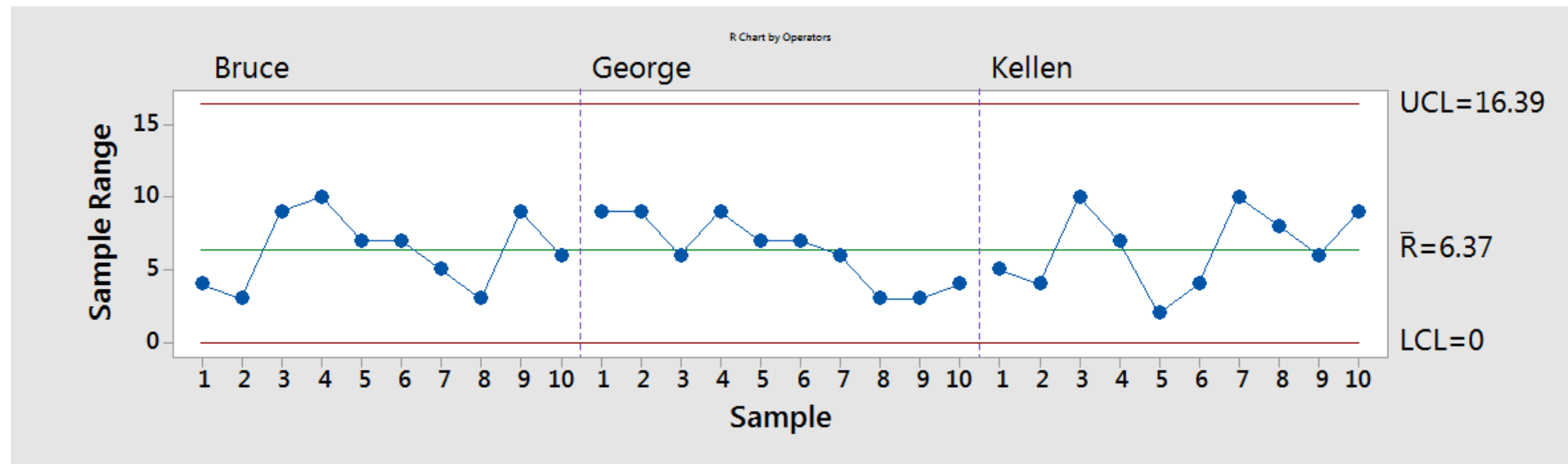
Can I trust my data? - Gage R&R

- ▶ Gage Repeatability & Reproducibility Study is used to determine if *Measurement Variation* is too high.



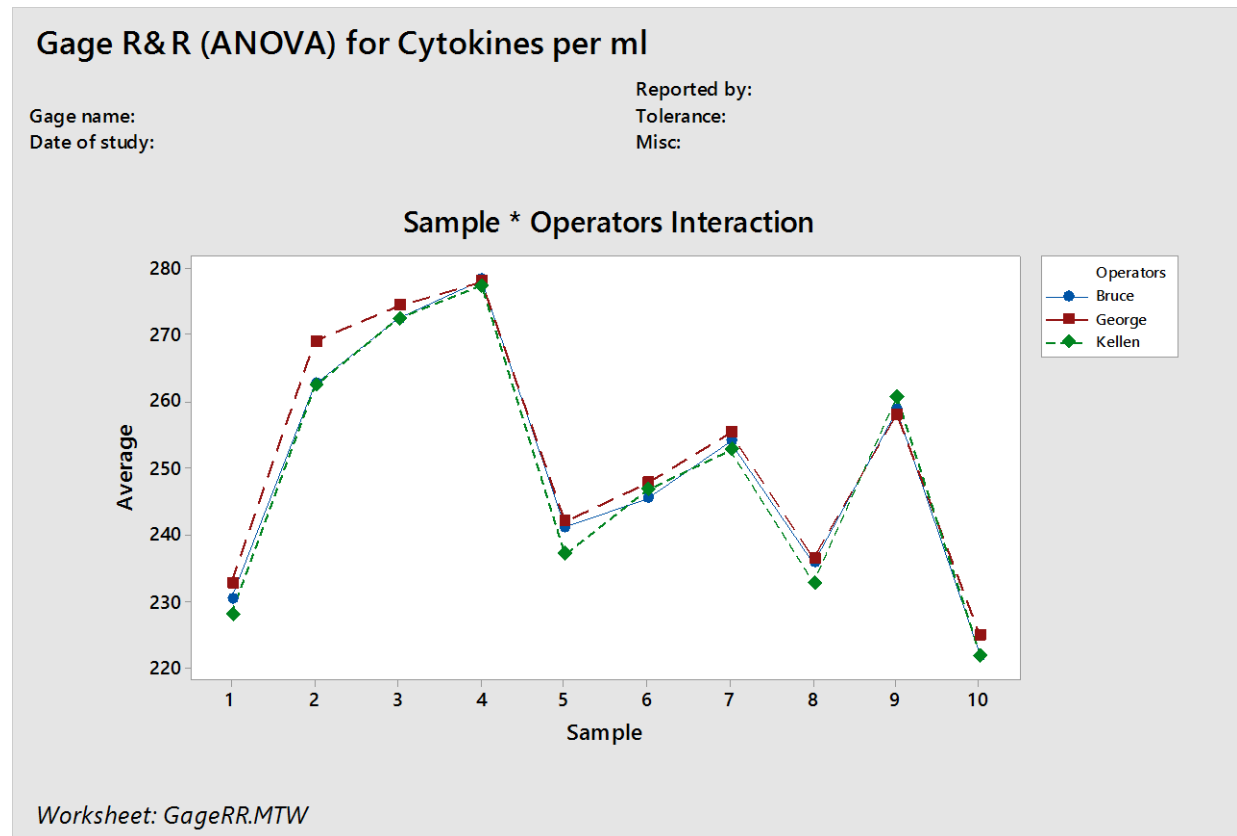
Can I trust my data? - Gage R&R

- ▶ Too much measurement error? Improve the measuring system.



Can I trust my data? - Gage R&R

- ▶ Too much measurement error? Improve the measuring system.



Regression

- ▶ Additional data were collected at doses of 1000, 1100, 1200, 1300, and 1400 mg. Determine the dose needed to get the expected protein reduction to 20%.

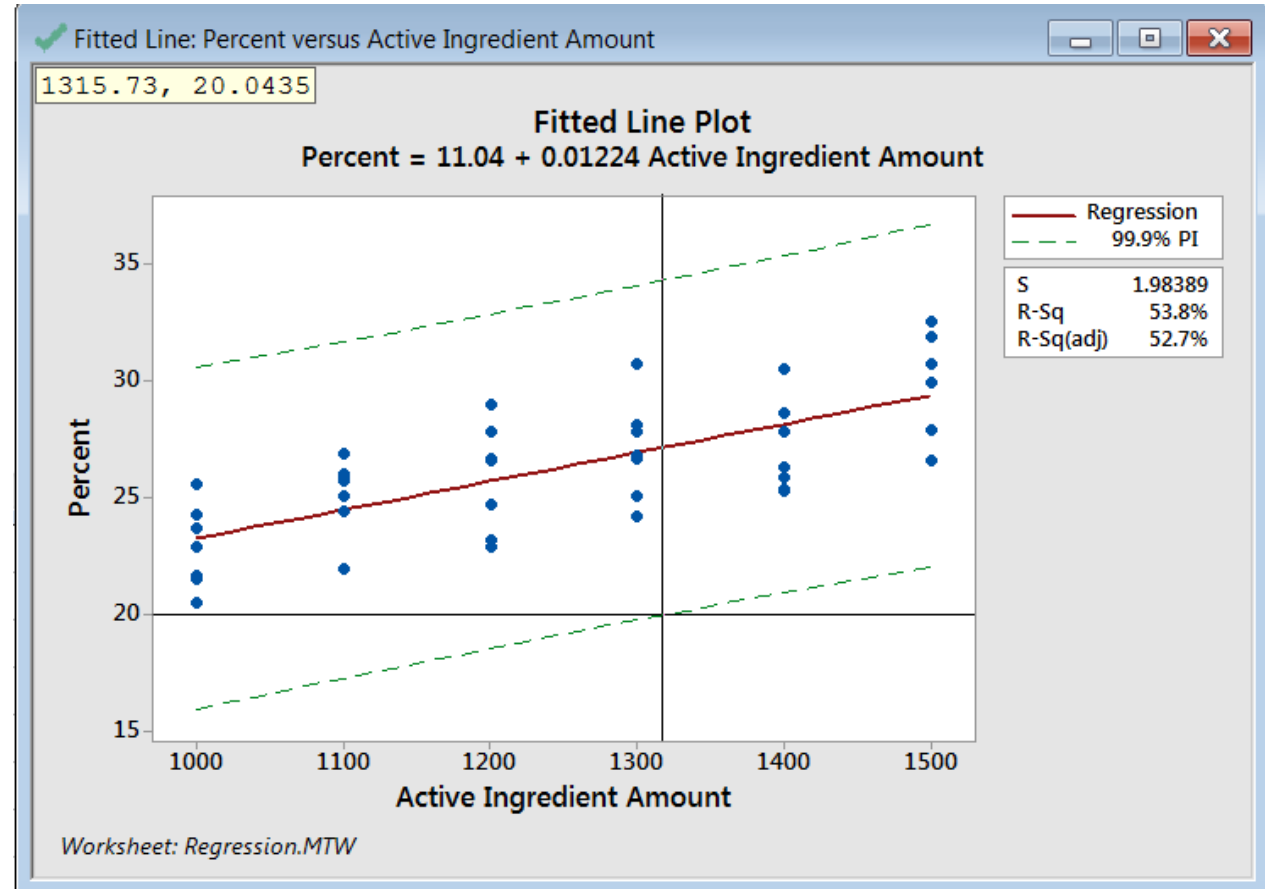
Active Ingredient	Protein reduction (%)
1000	21.7
1000	24.3
1000	25.6
1000	21.5
1000	22.9
1000	20.5
1000	23.7
1500	30.7
1500	30.7
1500	26.6
1500	27.9
1500	29.9
1500	31.9
1500	32.5
1100	26.9
1100	25.1
1100	26.0
1100	22.0
1100	24.4

Regression

- ▶ Regression analysis is a statistical process for estimating the relationships among variables.
- ▶ Regression analysis is widely used for prediction and forecasting.

Regression

- ▶ Determine the dose (active ingredient) needed to get the expected protein reduction to 20%.



Capability Analysis

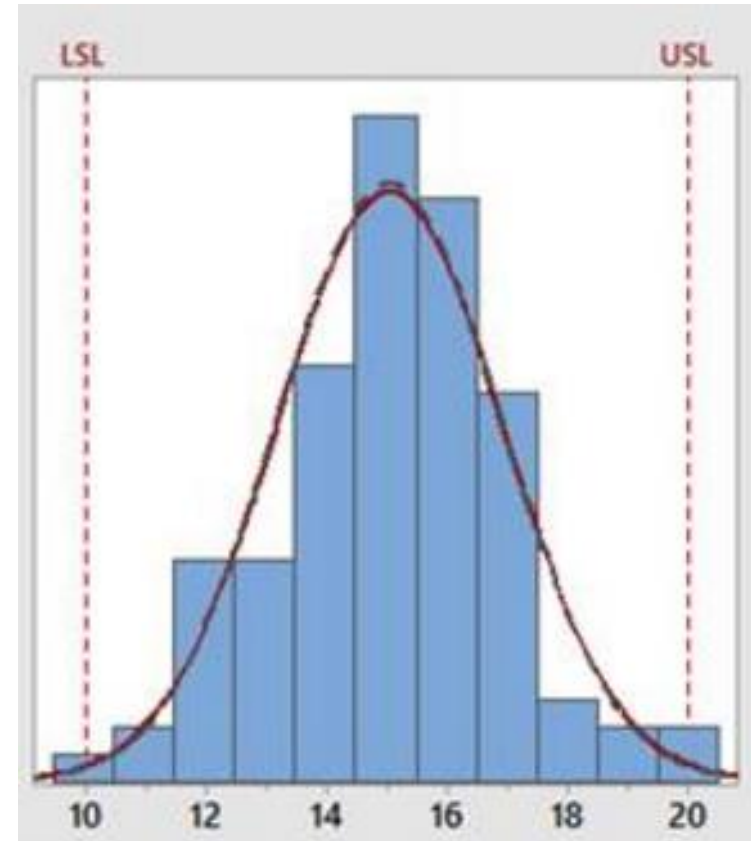
► Capability Analysis

- After the manufacturing process is scaled up, it is not feasible to measure how the drug reduces the cytokines in patients.
- How capable is the process to produce drugs with the active ingredient higher than 1315mg?

Subgroup	Active Ingredient Amount
Mon Shift 1	1331
Mon Shift 1	1339
Mon Shift 1	1332
Mon Shift 1	1341
Mon Shift 1	1338
Mon Shift 2	1342
Mon Shift 2	1338
Mon Shift 2	1334
Mon Shift 2	1352
Mon Shift 2	1339
Mon Shift 3	1335
Mon Shift 3	1336
Mon Shift 3	1342
Mon Shift 3	1341
Mon Shift 3	1339
Tues Shift 1	1330
Tues Shift 1	1337
Tues Shift 1	1329
Tues Shift 1	1337

Capability Analysis

- ▶ What is capability analysis?



Capability Analysis

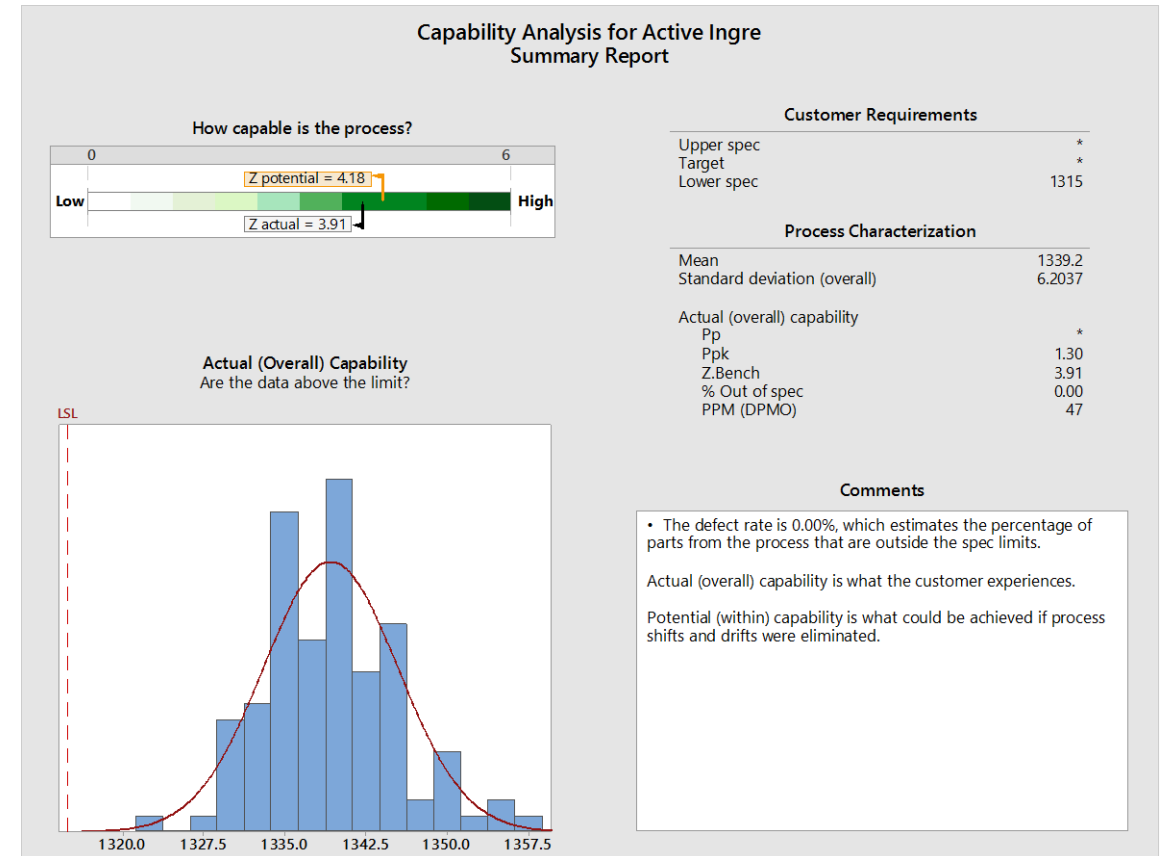
► When to use Capability Analysis

- The measurement system is reliable
- The process is in control

► Capability Analysis

- LSL = 1315

► Minitab Demo



Get a Plan and Document It

▶ Evidence of effective self-governance

- Describe how to calculate **sample sizes** for each test/analysis
- Specify the ***confidence level*** for statistical tests
- Describe the ***statistical techniques*** used
 - the type of control chart to use
 - the recommended subgroup size
 - the frequency of sampling
 - how out of control points are identified
 - how out of control points are to be handled
- Describe ***how to perform*** the analysis

Minitab

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