

Control Charting: Lessons Learned Along the Way Why, What, and How

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Why?

- Because it is required: ISO/IEC 17025 section 5.9 with numerous additional requirements within the AOAC Guidelines for Laboratories performing Microbiological and Chemical Analyses of Food and Pharmaceuticals
- Because it is a good idea: allows you to visualize changes in a method
- Done right, it can make calculation of measurement uncertainty easy

What to Control Chart

- In most cases, the answer is obvious; the value or percent recovery of the Laboratory Control Sample (LCS) that is run with each batch of samples
- But...what about qualitative methods? What about screening methods? What about methods that are estimates like Most Probable Number (MPN) methods?

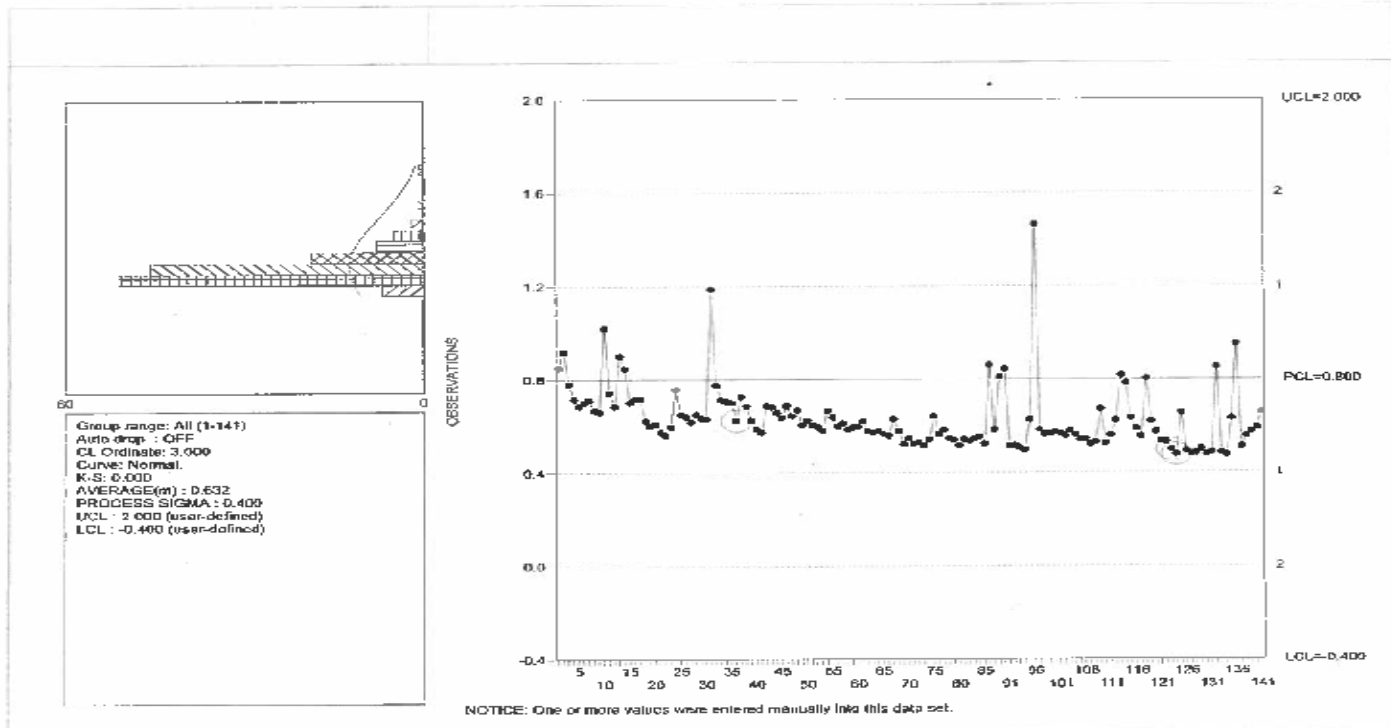
How to Determine Appropriate Control Chart Limits

- Fixed limits versus moving average limits
- Do I have to use $\pm 3SD$ for my control chart limits?
- How do I determine a limit for a screening method?
- How do I determine a limit for a qualitative method?

Qualitative Methods

- I have a method that is presence/absence, what do I control chart?
- This has to be evaluated on a case by case basis
- Our HPLC method for artificial colors is a presence/absence method based on a retention time match and a spectral match to the standard

Charting of Spectral Match



Screening Methods

- Most screening methods are based on an analyte exceeding some predetermined limit. The control sample itself should be at a level meaningful to the determination
- Usually, a positive sample from a screen is then confirmed using another method
- Much like control charting of qualitative methods, charting of screening methods has to be evaluated on a case by case basis
- Some questions to ask are: Does the upper limit matter? Does the lower limit matter? How good is my screening method? What level does the analyte have to be before I make a regulatory determination or go to a confirmation method

Aflatoxin Screening Control Limits

- A method used to screen out negative samples and reduce the number of samples requiring HPLC confirmation
- What do I want to control, false positives (high recoveries) or false negatives (low recoveries)?
- Do I care about the upper limit for the control chart? The upper control chart limit is not critical to this method
- Do I care about the lower control chart limit? The lower control chart limit is critical to this method
- Do I care about the average? No, not really

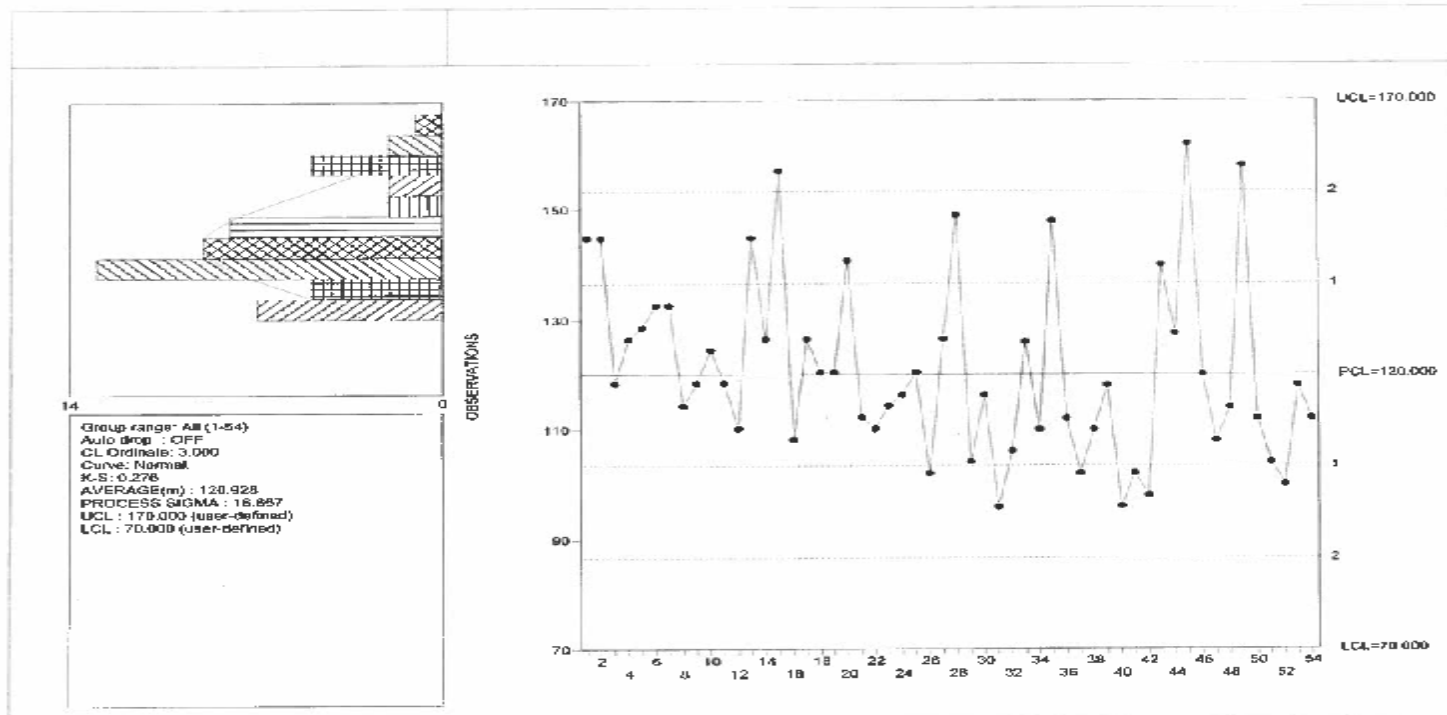
Aflatoxin Screening Facts

- The regulatory limit for corn and peanuts is 20ppb. Our control samples are corn and peanut butter at levels as close to 20ppb as we can find acceptable controls.
- Our screening method is an immuno affinity column cleanup with determination by a fluorometer. It specifies that any sample at 10ppb or higher will be confirmed by HPLC.

Aflatoxin Screening, Setting the Lower Control Limit

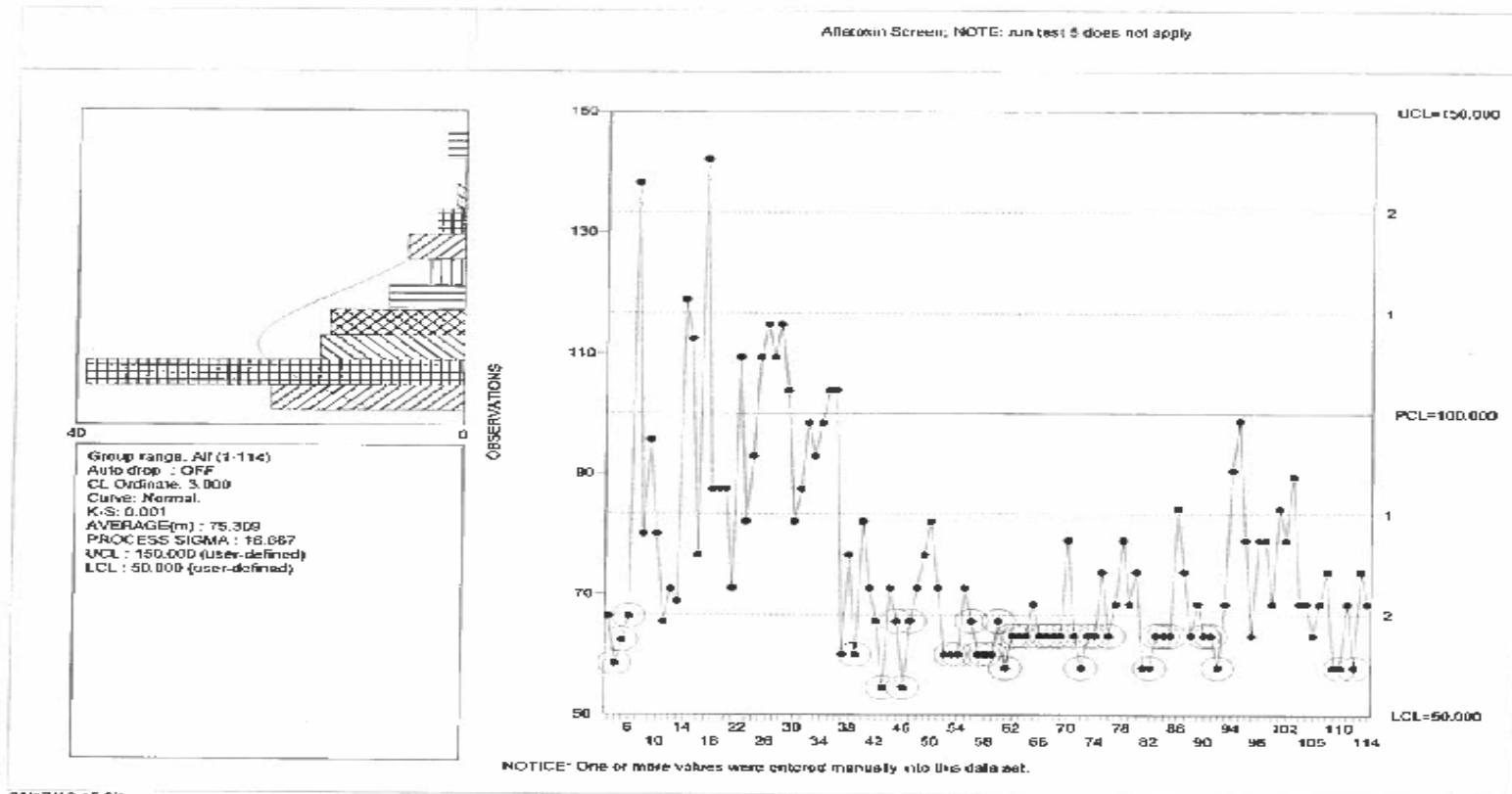
- Have I establish some critical value for the lower control limit? Yes! With the statement that all samples screened at or above 10ppb, which is 50% of the regulatory limit, a critical value was established.
- Does my lower limit have to be 50% recovery? No, if the method performs better than that, or there is a high bias, then your lower limit should be greater than 50% recovery.
- Does my lower limit have to be 50% recovery? Unless the criteria for which samples move on to confirmation is changed, there is no justification for setting your lower control limit below 50% recovery – it would no longer be fit for purpose

Control Chart for Aflatoxin in Peanut Butter



01/17/19 15:07
Method545_AflaScreen_peanuts.qdc: X Chart: Method545_AflaScreen_peanuts - Percent Recovery

Control Chart for Aflatoxin in Corn



01/17/18 15:07
 Method545_AflaScreen_Corn.qdc, X Chart: Method545_AflaScreen_com - Recovery

What to Control Chart for MPN Methods

- Our laboratory uses a commercially produced pellet of known value for the control sample
- We have tried control charting the log 10 value of the control sample, the percent recovery based on the log 10 value (from the expected value), and the number of positive MPN tubes (water samples only, no dilution).
- Each option for control charting MPN has its pros and cons – there is not a “best” method

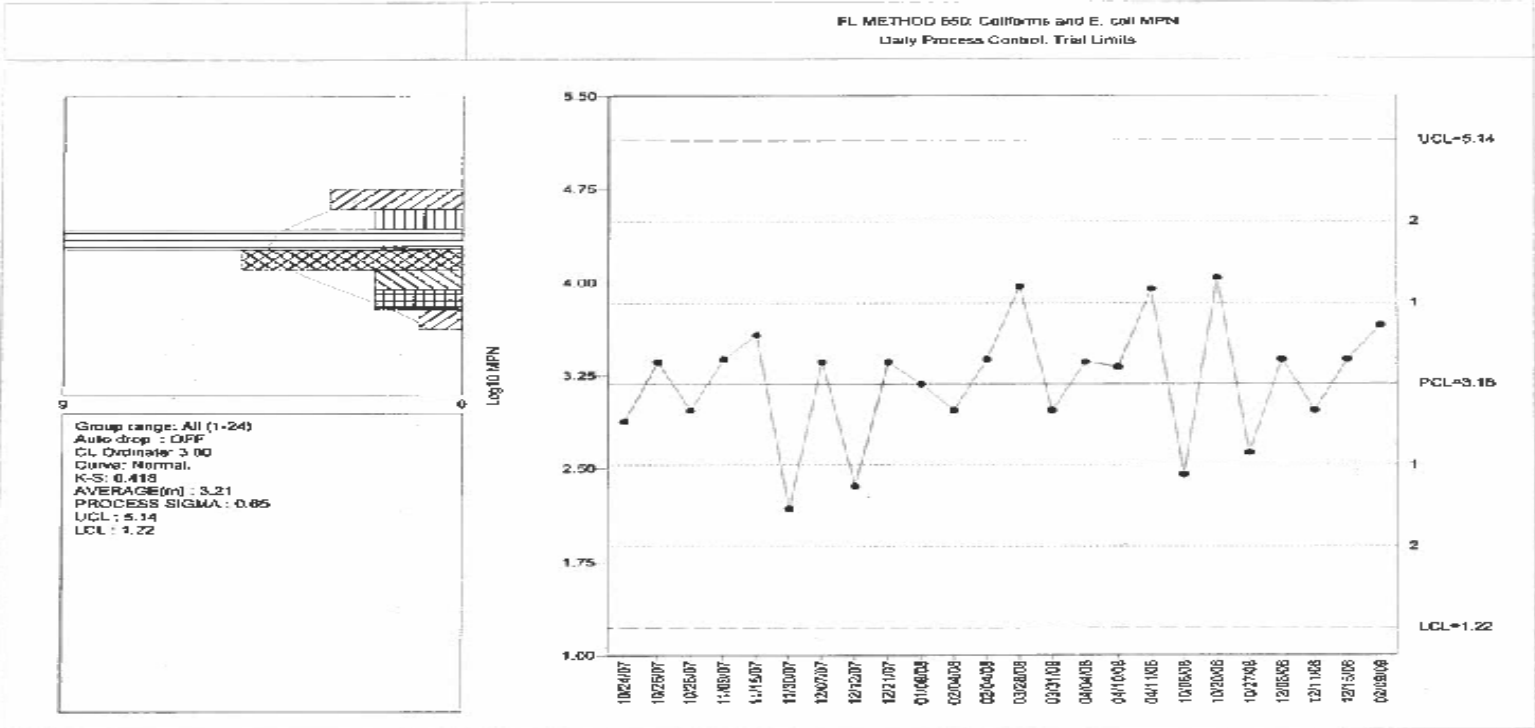
MPN Control Charting and Lessons Learned

- MPN is an estimate: “Most Probable Number”
- Add in variability from the pellets, especially if there are problems with the dissolution of the pellets or clumping
- Additional dilutions of the control that are not done to the customer samples can result in additional variation in the control that is not seen in the samples
- There are a finite number of possible answers so there tends to be “clusters” of the same result
- There is a ceiling beyond which there cannot be any other answer for a given dilution
- All of these factors combined cause the MPN control charts to behave differently than other control charts

Charting Log 10 value of MPN Results

- Pro: very simple for the analyst to enter the control values
- Con: Control Charts have to be changed when pellet lots change due to the change in expected value for the organism
- Con: This method can give very large apparent ranges
- Con: Does not give useful information if needed for calculation of MU

Log 10 MPN with High Variability: The Early Days

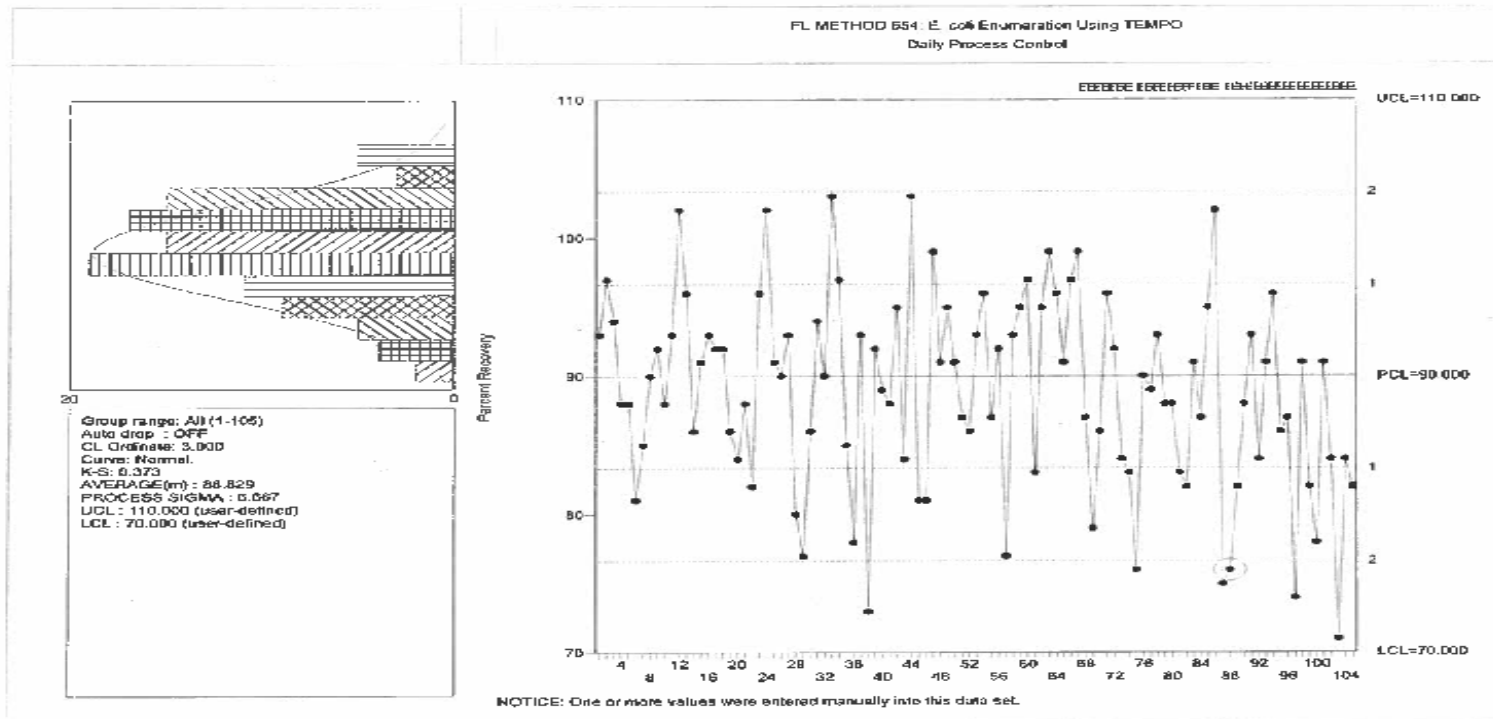


01/18/16 15:03
Method650_Cheril.qdc: X Chart: #Method650_Data - LOG(10)MPN

% Recovery from Log 10 values

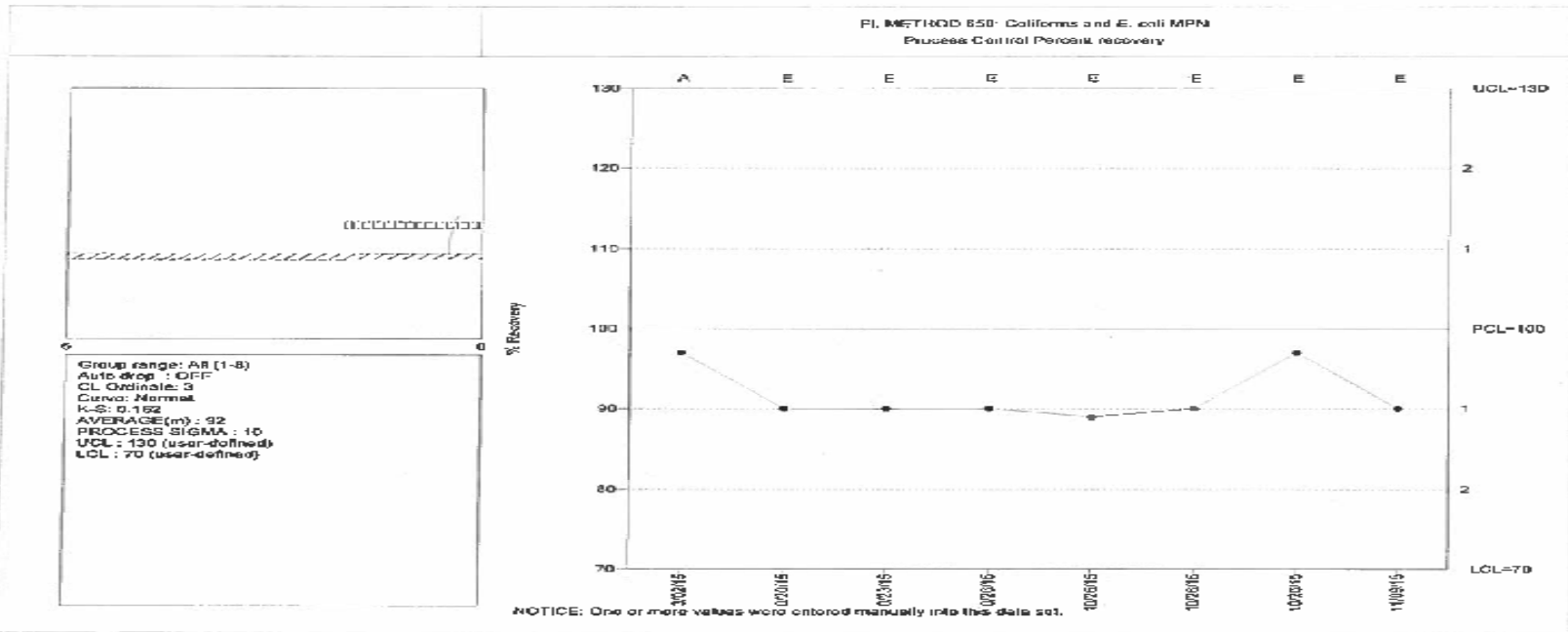
- Still simple to enter the control values, but does require a calculation and knowing the expected value
- Pro: Control Charts do not have to be changed when pellet lots change – that is accounted for in the calculation
- Calculating as % Recovery does smooth the chart though there can still be large apparent ranges
- Pro: This can be used to help with determination of Measurement Uncertainty (MU) if needed

Normal Distribution using % Recovery with MPN



01/20/16 13:09
Method654_Percent_Recovery_Chart.qdc: X Chart: Method654_Percent_Recovery_Data - PERCENT RECOV.

% Recovery Chart for MPN: Today Use of CRM for Control Sample

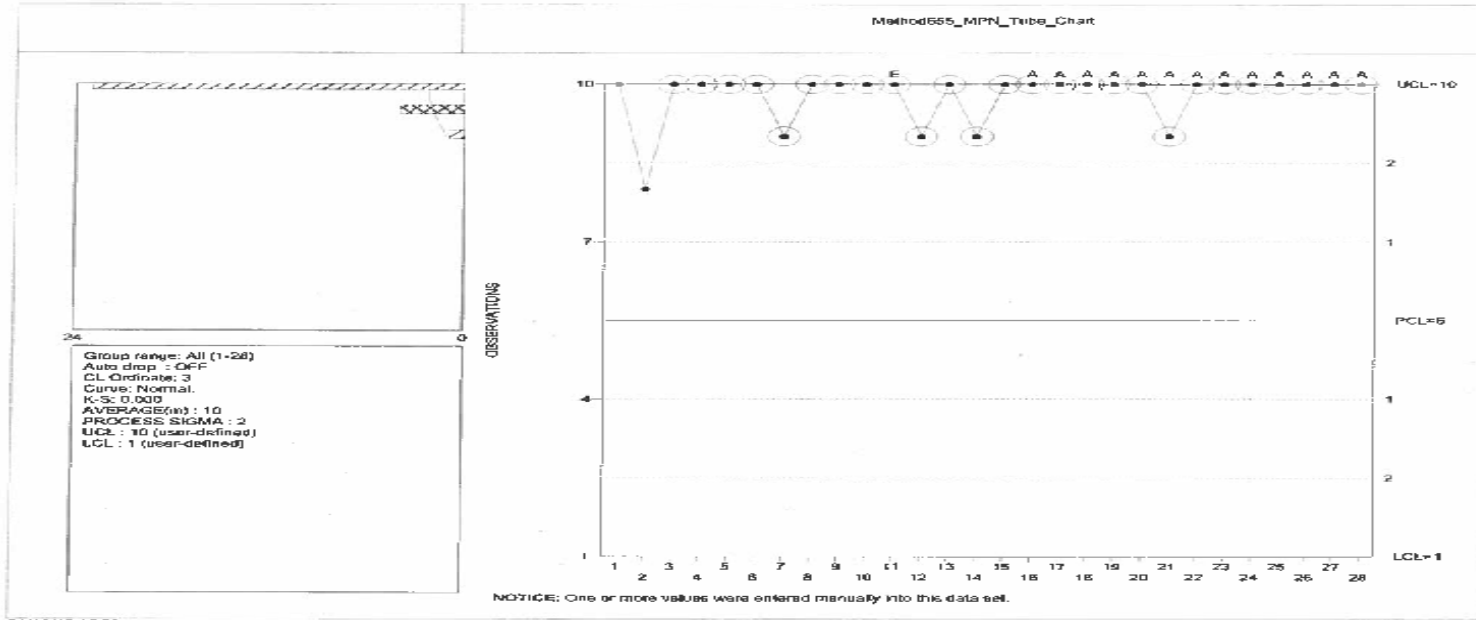


DW16M6 1526
 Method650_Recovery_Chart.qxd: X Chart: Method650_Recovery_Data - PERCENT RECDV.

Number of Positive Tubes in MPN

- Used for our bottled and vended water method
- MPN is used if samples are not suitable for analysis by membrane filtration
- Water has a very low regulatory limit
- Control sample concentration is low, but still turns most MPN tubes positive
- Control chart is of limited use for the calculation of MU

Control Chart of Number of Positive MPN Tubes



01/16/18 15:39
 Method655_MPN_Tube_Chart.qdc X Chart: Method655_MPN_Tube_Data - POS CONTRL

Dealing with Exceptions to Control Chart Requirements

- For my laboratory, the main SOP governing Control Charting gives general guidelines and those rules are programmed into the control chart application (circles are trending, squares are out of control)
- The Control Chart SOP allows for exceptions to be specified in specific method SOPs
- The method SOP will state if there is an exemption to the requirements of the Control Charting SOP
- Analysts refer to the method SOPs more often than they do to the Control Chart SOP; the method SOP will tell them if they can ignore a trending point – out of control points always require a corrective action