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TRENDING SMARTER

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Unlocking the Hidden Value in EM Data Beyond Alert/Action Limits

Environmental monitoring (EM) programs are designed to demonstrate a facility's ongoing state of control, yet the microbiological data they generate are inherently semi-quantitative, sparse, and often zero-inflated. Guidance such as USP <1116>, EU Annex 1, and PDA TR13 recognize that these data rarely follow a normal distribution and that conventional statistics based on the mean and standard deviation can misrepresent process behavior. Reliance on fixed alert and action limits, which are themselves constructs derived from historical data, can therefore obscure early signs of drift. A more meaningful assessment of control requires evaluating overall patterns of recovery rather than isolated excursions, aligning trending practices with the principles of risk-based, data-driven control.

WHY DOES EXCURSION TRENDING FALL SHORT?

• Microbiological EM data are non-normal and often contain an "inflated" number of zeros.
• Action/alert limits are constructs: their value depends on the quality and quantity of historical data supporting them.
• Excursion-based trending can miss sub-threshold drifts and over react to random single events.

A modern EM program emphasizes trend signals that reveal the true state of cleanroom control rather than only threshold breaches.

OBJECTIVES

• Understand regulatory expectations for trending in EM (USP <1116>, PDA TR13, EU Annex 1).
• Distinguish compliance vs. best practice vs. sound statistical science in EM trending.
• Recognize the limitations of excursion-only trending.
• Apply metrics — such as Contamination Recovery Rate (CRR%) and percentile-based alert levels — to gain earlier, more meaningful insights into cleanroom performance.
• See examples of these methods in action.

STATISTICAL PRETEXT

Many EM programs have borrowed traditional statistical ("parametric") rules from manufacturing, in which limits are often calculated as the mean plus 2–3 standard deviations (σ) of historical counts.

This approach assumes the underlying data are continuous and normally distributed, so excursions above the calculated limit signal an unusual event.

Microbiological EM data, however, are discrete counts, sparse, and often zero-inflated, so the assumptions of normality and constant variance do not hold. This usually looks like microbiologists attempting to "clean up" or "normalize" EM data prior to trending, which is cumbersome and can distort the real frequency structure and hide true signals.

As noted in PDA TR13 and USP <1116>, this can produce unstable limits that either over-react to single recoveries or miss slow drifts in recovery frequency.

Modern trending therefore emphasizes distribution-appropriate ("non-parametric") methods such as percentile-based thresholds and contamination-recovery rates (CRR %), which are more stable for microbiological recovery data sets.

Microbial recoveries in EM are rare-event counts that follow Poisson-like or zero-inflated distributions, not a Gaussian curve. Because variance scales with the mean, conventional mean ± σ thresholds are unstable at low incidence. CRR % — the proportion of samples with any growth — is less sensitive to assay counting variability and normalizes performance across sites. Percentile-based limits (e.g., 95th for alert, 99th for action) use the actual distribution of historical data, enabling detection of incremental upward drift within the "normal" range before excursions occur. Together these methods give a more realistic picture of state-of-control.

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CITATIONS

1. United States Pharmacopeia (USP). General Chapter <1116> Microbiological Control and Monitoring of Aseptic Processing Environments. In: USP–NF. Rockville, MD: The United States Pharmacopeial Convention.
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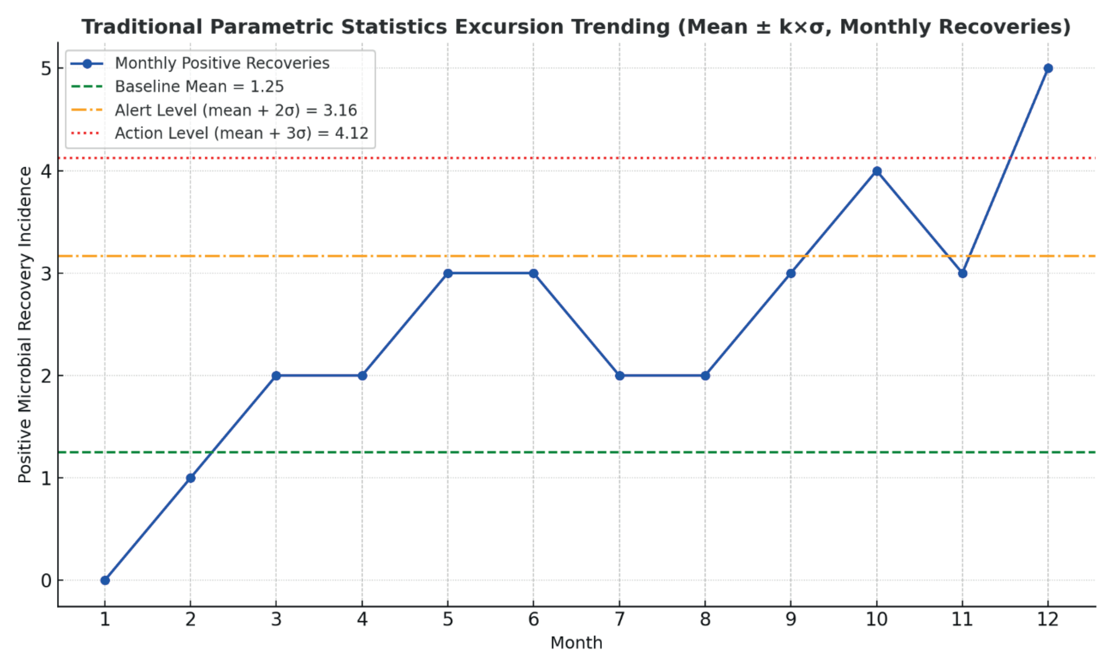
REGULATIONS ON TRENDING

REGULATION	NOTES ON TRENDING FOCUS
EU GMP Annex 1 (2022) §9.9-9.13	Requires facilities to establish, maintain and periodically review alert/action levels using trend data, monitor for increasing excursions, consecutive alerts, recurring post-maintenance excursions, and shifts in micro-flora.
USP<1116>	Focuses on recovery rates and trend signals over excursions; recommends tracking detection frequency and adjusting limits when trends rise above historical capability.
PDA TR13	Explains limits of parametric mean ± σ rules; endorses percentiles, CRR% and CCC charts for EM data

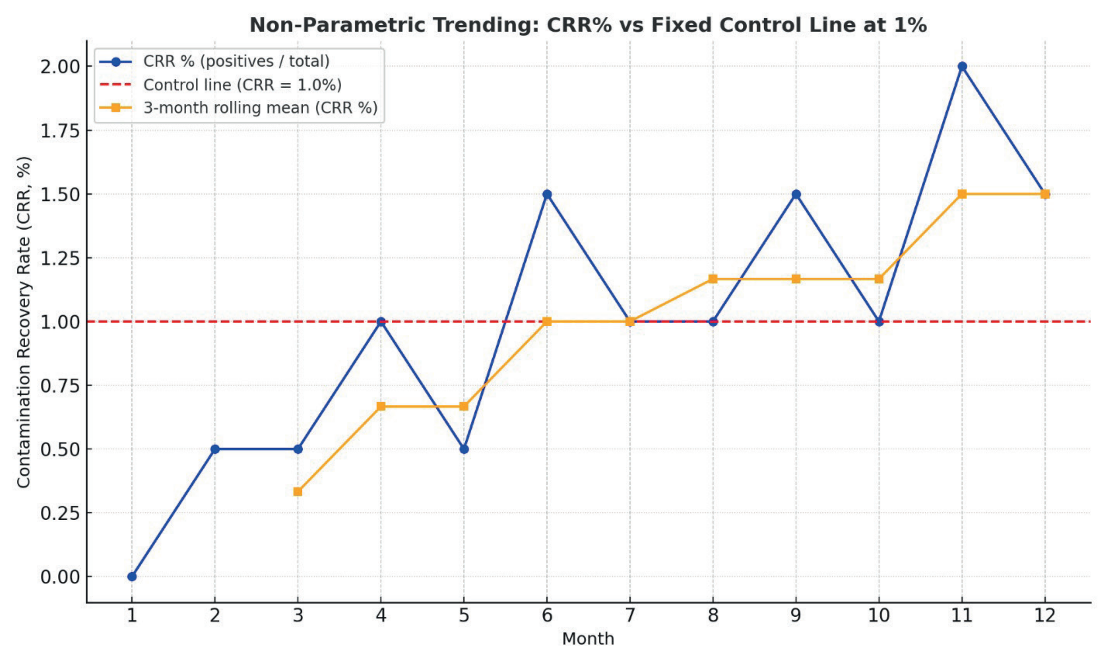
PARAMETRIC VS NON-PARAMETRIC



WHAT IT SHOWS?

• Monthly positive recoveries (#) look "in control" until late in the year.
• Alert and Action lines are fixed from an early baseline (first 4 months).
• The slow drift is largely invisible until the tail end — classic blind spot of mean±σ with low-count data.

PARAMETRIC VS NON-PARAMETRIC



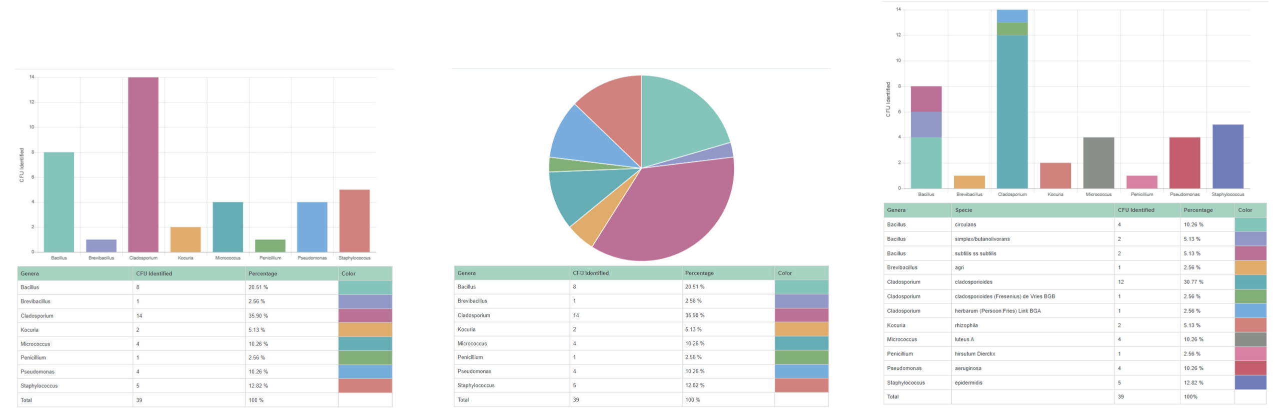
WHAT IT SHOWS?

• CRR % (positive / total) creeps up month by month.
• A baseline 95th percentile (first 4 months) is crossed much earlier than any parametric "action" threshold.
• A simple 3-month rolling line reinforces the upward drift — an intuitive, defendable non-parametric signal.

MORE TRENDING TOOLS

MICROBIAL RECOVERY IDENTIFICATION:

These figures summarize the flora recovered from EM over 1 year: figure A shows absolute counts by genus, figure B shows percent composition, and figure C breaks key genera into species. Together they reveal dominant organisms and shifts in the micro-ecology—e.g., increases in spore-formers/molds or Gram-negatives. Recurrent species in the same area or with the same activity suggest harborage sites or operator linkage and help target disinfectants, training, and CAPAs. For interpretation, pair ID composition with CRR% and ID rate (IDs ÷ positive samples) to avoid bias from changing sample volumes or identification frequency and to detect early drift before excursions rise.



STATISTICS PER POINT

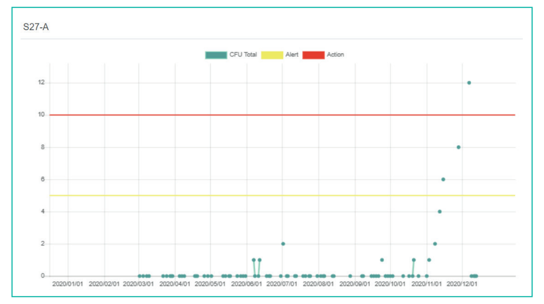
Do you notice something here? Looking at the four Grade B active-air points at this facility side by side, one site isn't behaving like the others. S27-A shows episodic spikes (only point with actions, higher alert rate, larger SD, and the highest 98th/99th percentiles), and tables like these can make it easy to spot these incongruencies.

Point	Samples	Equal to 0	Greater than 0	Alerts	Actions	Mean value*	Standard deviation*	Mean + 3 sigma*	95th percentile*	98th percentile*	99th percentile*
S21-A	284	227 (79.93%)	57 (20.07%)	1 (0.35%)	0 (0.00%)	0.31	0.71	2.44	2	2	3
S24-A	284	251 (88.38%)	33 (11.62%)	2 (0.70%)	0 (0.00%)	0.21	0.75	2.46	2	2	4
S26-A	77	68 (88.31%)	9 (11.69%)	0 (0.00%)	0 (0.00%)	0.14	0.42	1.40	1	2	2
S27-A	77	66 (85.71%)	11 (14.29%)	2 (2.60%)	1 (1.30%)	0.36	1.26	4.14	2	6	8
Total	**722**	**612 (84.76%)**	**110 (15.24%)**	**5 (0.69%)**	**1 (0.14%)**	**0.26**	**0.78**	**2.60**	**2**	**2**	**3**

* Value obtained using only those values that are smaller than the action limit

TREND PER POINT

FIGURE 5 This Trend Per Point graph plots each recovery against the site's alert (yellow) and action (red) lines, letting us drill into how the point behaves over time. For most of the year S27-A shows increasing sub-alert positives (1–2 CFU) with occasional small spikes--evidence of a drift that is not obvious until Q4 when an action level is finally hit. If we apply sub-alert trending—e.g., CRR% (fraction of samples >0) and percentile limits (95th-99th computed on sub-action data)--the rise in detection frequency would flag this point months earlier, prompting investigation before the late-year excursions appear.



TREND PER POINT & PERSON

These data graphs (figures 6-9) track a single operator's body sites (e.g., waist, right/left hand, chest) over time with the site's alert/action lines. By adding sub-alert metrics—CRR% and percentile thresholds—you can detect a rising hit frequency well before any excursion, then verify pre/post-training impact. Pair with IDs to link specific flora to behaviors and target CAPAs.