

The Age of Digital Transformation: for Risk-Based Contamination Control Strategies Based on Annex 1

Corinne Cleary

Product Specialist: Technical Processes and Innovation

Novatek International

Email: Corinne.Cleary@ntint.com

LinkedIn: [linkedin.com/in/corinne-cleary-9baa6725/](https://www.linkedin.com/in/corinne-cleary-9baa6725/)

Phone: 1-514-686-5135

Over 10 years experience defining User Requirements for Pharmaceutical and Biotech





Agenda

- Understanding True Digital Transformation, including Digital vs Digitalized Data
- Understanding how Annex 1 supports digitalized solutions
- Linking elements of contamination control through digitalization, including data correlation for trending and pattern recognition
- Learning to source technological tools
- Applying digitalization strategies to contamination control data
- Identifying process specific points to consider, including data sources, data conversions and steps to a true transformation under Annex 1
- Identifying company/process transformation risks and developing appropriate counter measures
- Understanding Data Integrity considerations in both a CCS and for new technological tools



Digitization:

- conversion of paper-based records to digital records

Digitalization:

- Digitalization goes beyond this to transform the way that businesses operate by leveraging the power of digital technologies to optimize processes, increase efficiency, and improve decision-making.
- Digitalization uses advanced analytics to analyze large volumes of contamination control relevant data, the adoption of blockchain technology for secure data sharing and tracking, and the use of artificial intelligence (AI) and robotics to improve manufacturing and supply chain operations

Digitized vs Digitalized Data



- Covid Impact
 - need for digital transformation

Digitized vs Digitalized Data

- Benefits
 - Centralized data access
 - Data Correlation
 - Level of Data Analysis
 - Efficiency of Data Management and Operations
 - Real Time Monitoring and Immediate Detection of contamination events
 - Preventive measures and Pattern recognition
 - Compliance Considerations
 - Productivity and Reduced Costs
 - Integration and Interfacing



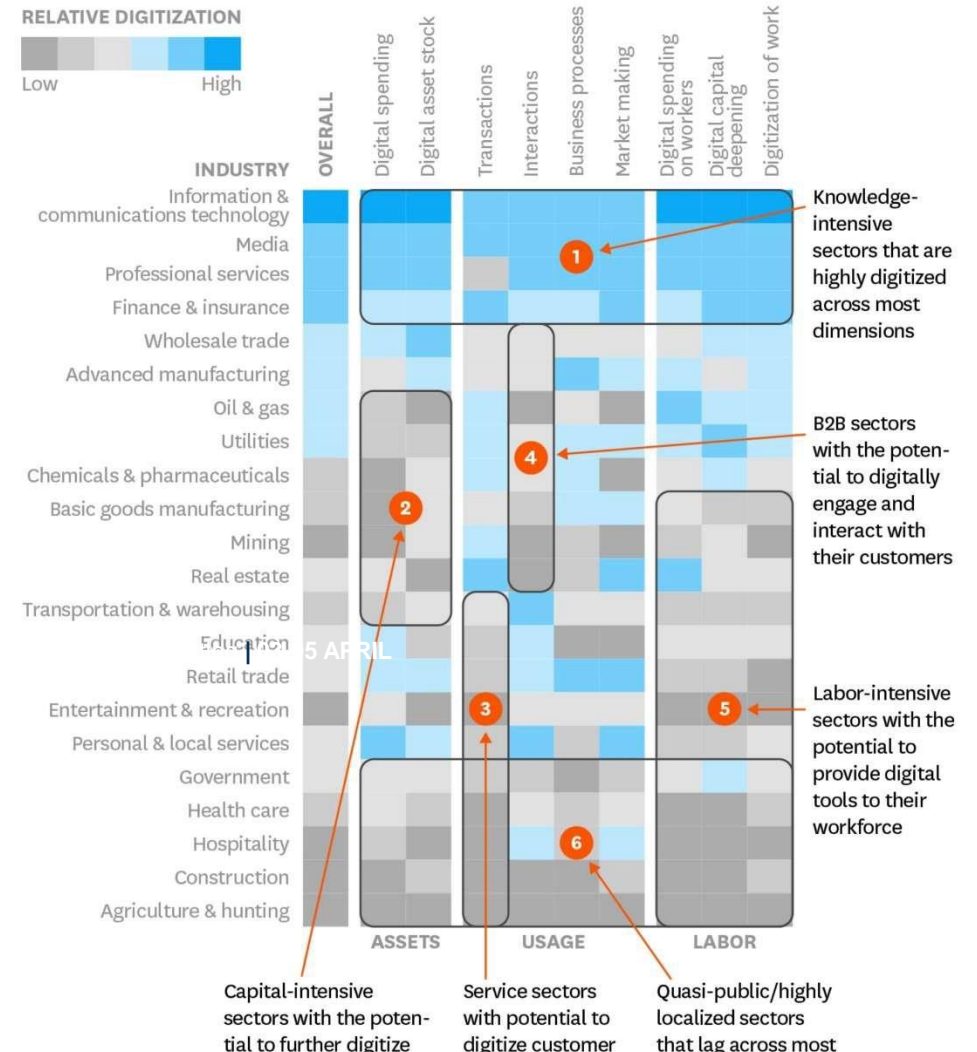
Organizational Impact

Some of the most common organizational barriers to digital transformation are:

- unclear vision and objective of digital transformation.
- lack of management understanding, knowledge and experience,.
- lack of leadership skills.
- lack of organizational agility, rewards and incentives that are not aligned to digital transformation.
- unclear measurement and rewarding system.
- lack of employee' involvement and engagement
- employee' resistance to change.

How Digitally Advanced Is Your Sector?

An analysis of digital assets, usage, and labor.



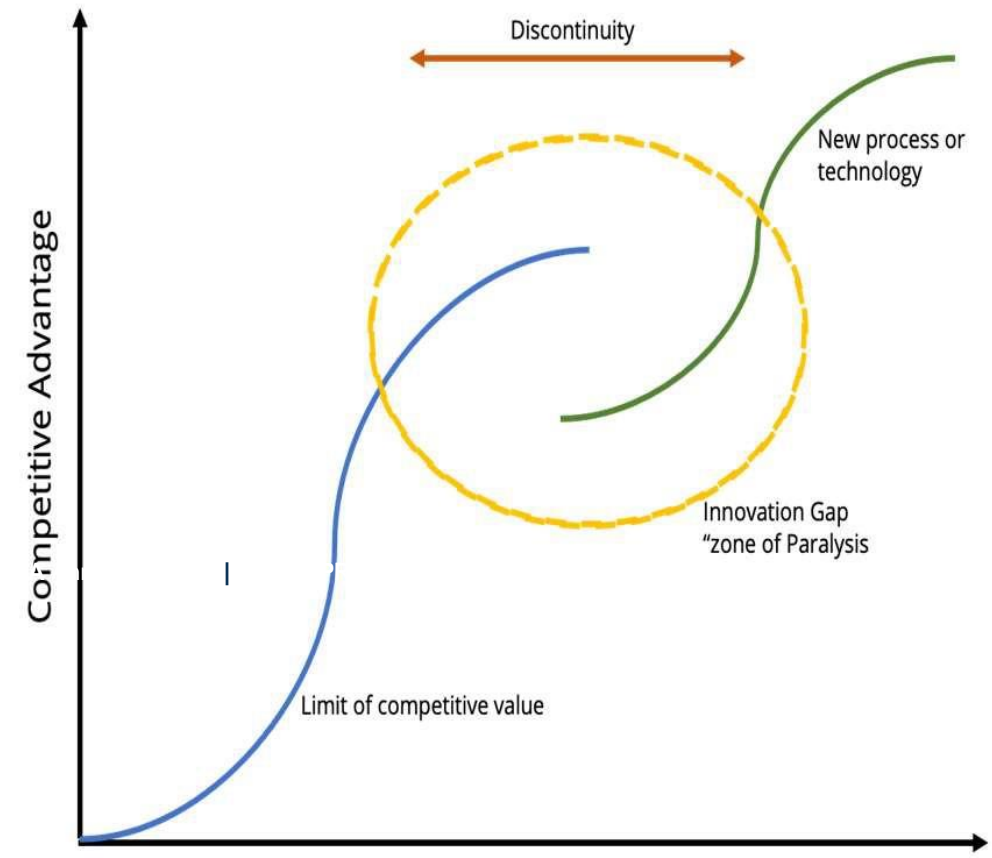


The need for new digital technologies in life science corporations, quality organisations, is no longer a point of discussion. In fact, with data being all-present companies are exploring big data strategies and in doing so they are discovering facts they didn't know before.

Yet, at the same time, budget constraints, sustainability objectives, faster developments of products and services remain leading in strategic decision making.

Investments in new technologies are still mostly driven by gut feeling, old paradigms and beliefs.

- By sticking with them they 'Can force continued investment in the original product category, blinding developers to alternative ways of thinking,' -Michael H. Elliot
- 'Creating a zone of paralysis or innovation gap that in today's complex and extremely fast-moving global business environment is almost impossible to catch-up if not recognized early enough.' – Prof. Cor Molenaar.



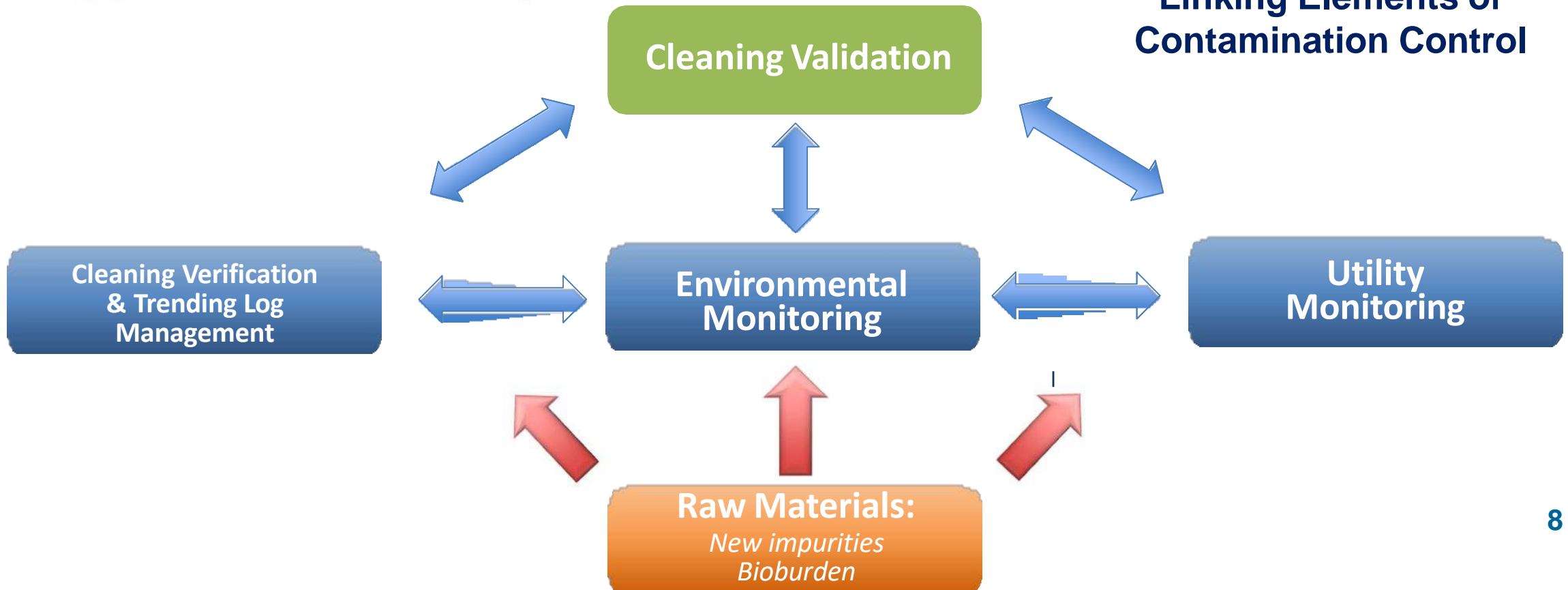
Digitization for quality management / control



Total Contamination Control Strategy

Not an isolated process

Linking Elements of
Contamination Control





Steps for True Digital Transformation

1. Assess the current state
1. Define digital transformation goals including holistic, risk-based URS
 - Use SMEs to identify process workflow for all CC elements
 - Identify data management risks
 - Create URS according to the process and risks identified
 - Ensure URS does not include design requirements
2. Identify data sources for all sites and all elements of CC
 - Facility design and activities
 - Equipment
 - Personnel
 - Utilities
 - Premises
 - Raw Materials & Excipients
 - Manufacturing Process
 - Environment (air, particle, micro, gas, cleanroom classification)
 - Supply chain

Steps for True Digital Transformation

4. Choose data management, analysis and AI solution(s)
5. Develop a detailed process and data conversion plan including available resources and responsible team
6. Rollout digital transformation solutions in achievable phases
7. Monitor and refine

Create both current and future workflows for all contamination control relevant processes. For each workflow step that includes data management, identify the data source, responsible group, and other relevant parameters such as correlation parameters and time spent managing the data. For example:

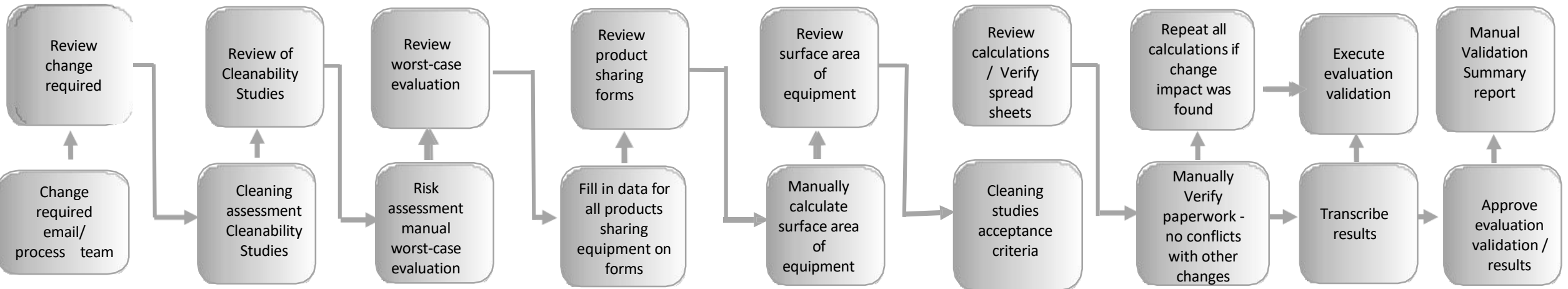
Current State: EM sampling program:
Responsible Department: *QC Micro* Data Source: *Paper Form in QMS*
Responsible Group: *Micro supervisors* Time Spent: *0.5 min/sample site weekly*

Future State: EM sampling program:
Responsible Department: *QC Micro* Data Source: *Automated CC solution software*
Responsible Group: *Micro supervisors* Time Spent: *0.5 min/sample site quarterly*
Data Correlation: *LIMS release data and QMS investigation*

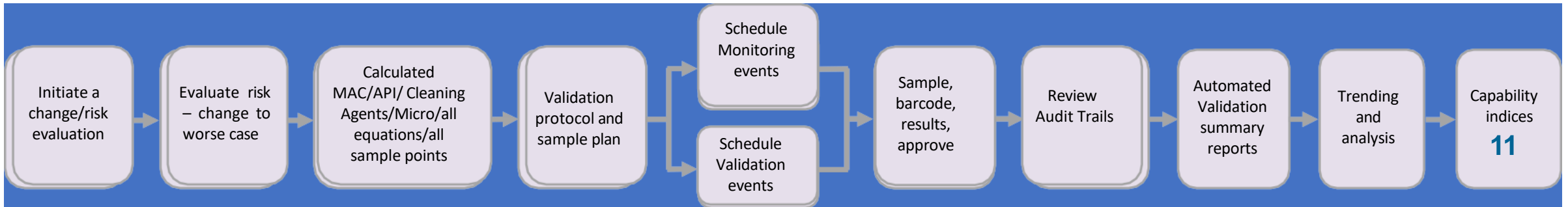
Identifying Data Sources

Cleaning Validation Current State vs Digitalized State

Current State



Digitalized State





Sourcing Tech Tools

- Conduct research of available tools and technologies
 - Online forums
 - Conferences
- Work with technology vendors
 - Partner with your tech vendors
- Leverage industry organizations such as PDA
 - Consult for trusted industry tools as well as up and coming technologies
- Consider regulatory guidance
 - E.g., special considerations for data integrity compliance
- Consider scope of resources available
 - E.g., out of the box or configurable systems



Annex 1 Revision & Digital Solutions

- Focus on risk-based approaches to contamination control
- Holistic approach to CCS
- Focus on Data Integrity
- Guidance on the use of Advanced Technologies, including automated monitoring and control systems

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How does Annex 1 Support Digitalized Solutions?



REGULATIONS

EU Annex 1, Revision 2020:

- The development of the CCS requires thorough technical and process knowledge.
- Potential sources of contamination are attributable to microbial and cellular debris (e.g. pyrogen, endotoxins)
- Particulate matter (e.g. glass and other visible and sub-visible particulates).



REGULATIONS

EU Annex 1, Revision 2020:

Elements to be considered within a documented CCS should include (but are not limited to):

- Prevention
- Trending,
- Investigation,
- Corrective and preventive actions (CAPA),
- Root cause determination
- and the need for more comprehensive investigational tools.





REGULATIONS

EU Annex 1, Revision 2020:

Equipment monitoring requirements should be defined in “user requirements specifications” and during early stages of development, and confirmed during qualification.

Process and equipment alarm events should be reviewed and approved and evaluated for trends.

The frequency at which alarms are assessed should be based on their criticality (with critical alarms reviewed immediately).



REGULATIONS

EU Annex 1, Revision 2020:

Results for critical parameters and critical quality attributes of high risk utilities should be subject to regular trend analysis to ensure that system capabilities remain appropriate.



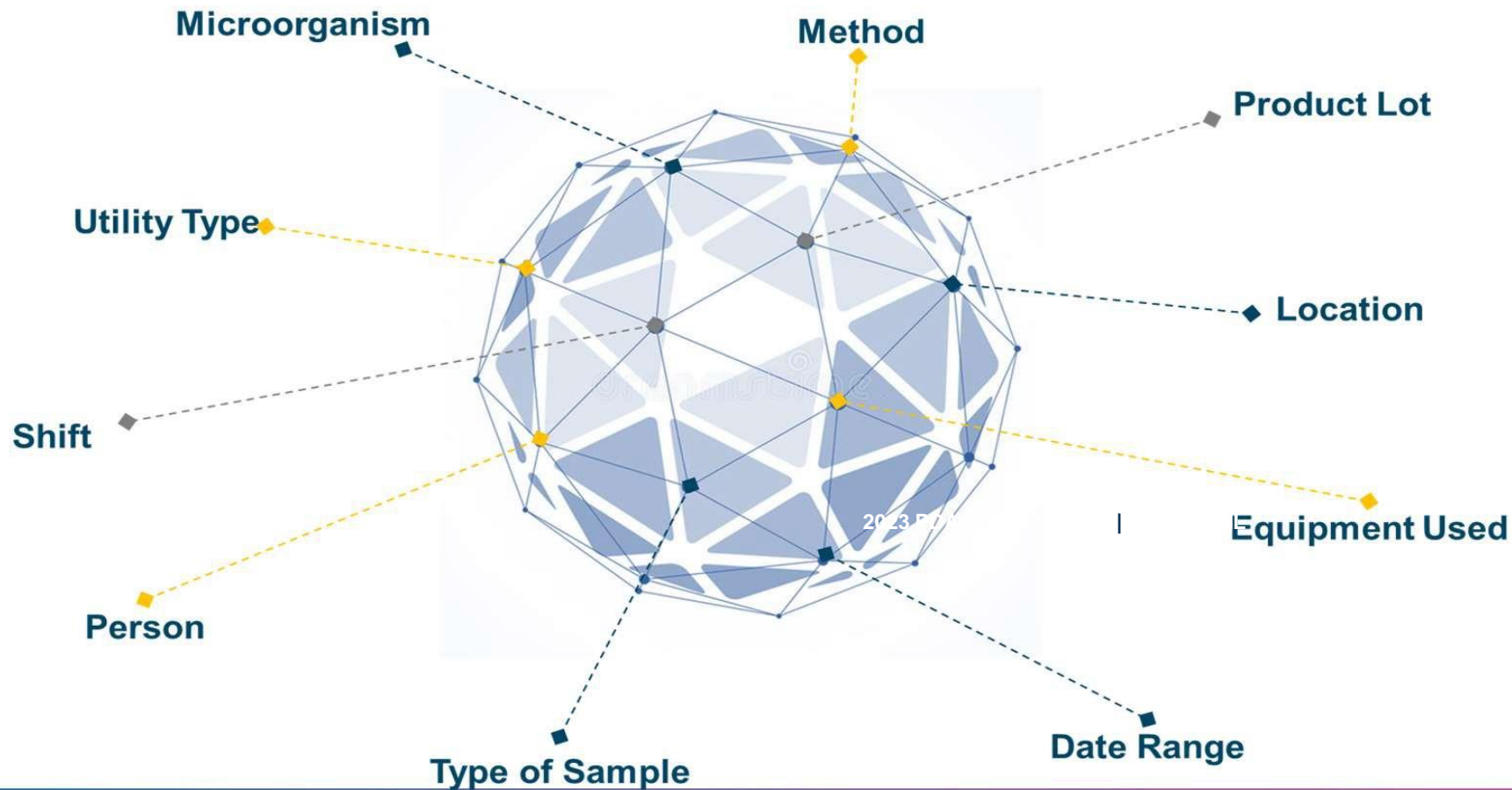


Strategy - Digitilization

- Enforcing Best Practices and CCS
- Automating Worst Case Analysis/Highest Risk Product/APIs
- Identifying High Risk Areas/Equipment Areas
- Automating HBELs calculations (MSC/MACO)
- Dirty Hold Time & Clean Hold Time Trends
- Analysis for Root Cause Determination
- Automated Utility and EM excursion notifications
- Digitizing HVAC filter qualification



Contamination Control Multifaceted Trending





Strategy - Powerful Trending Tools

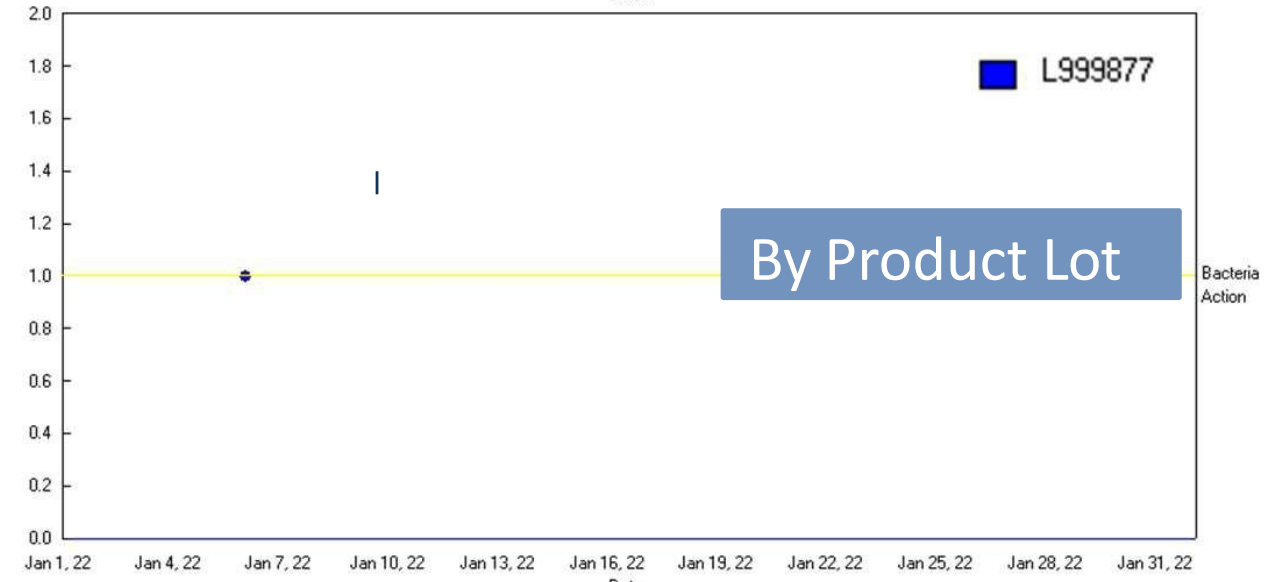
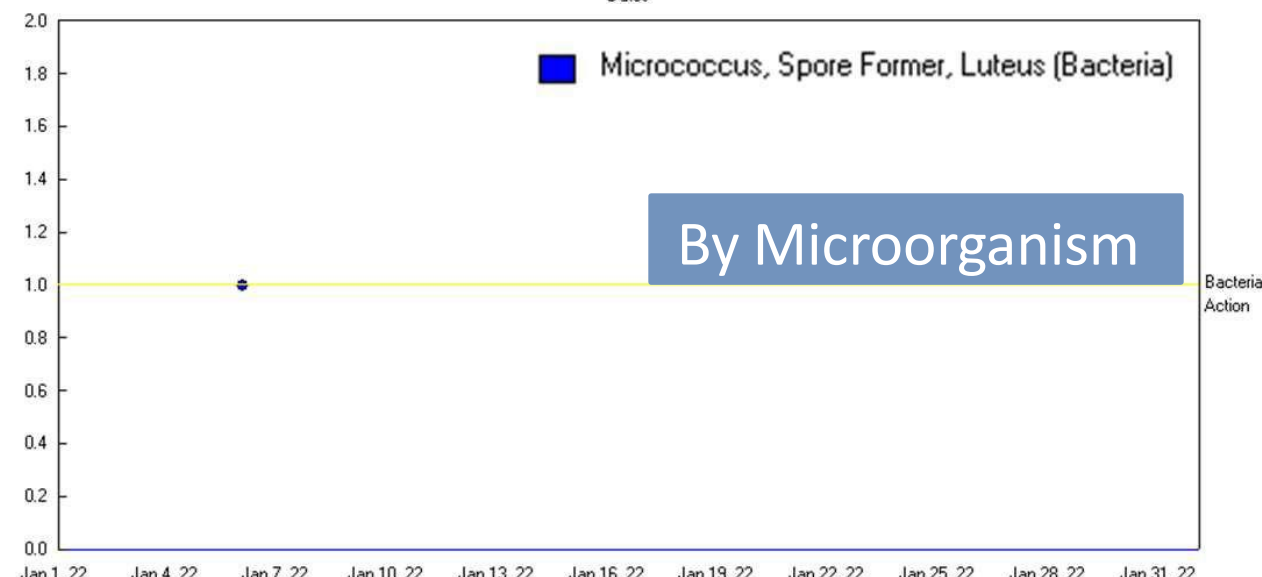
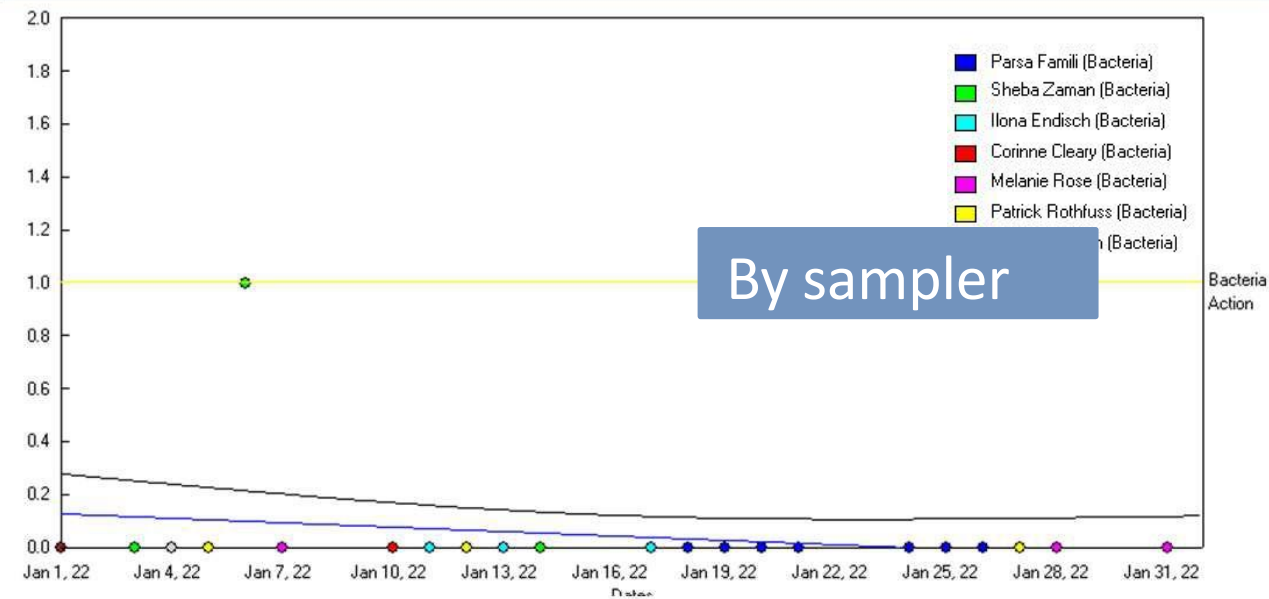
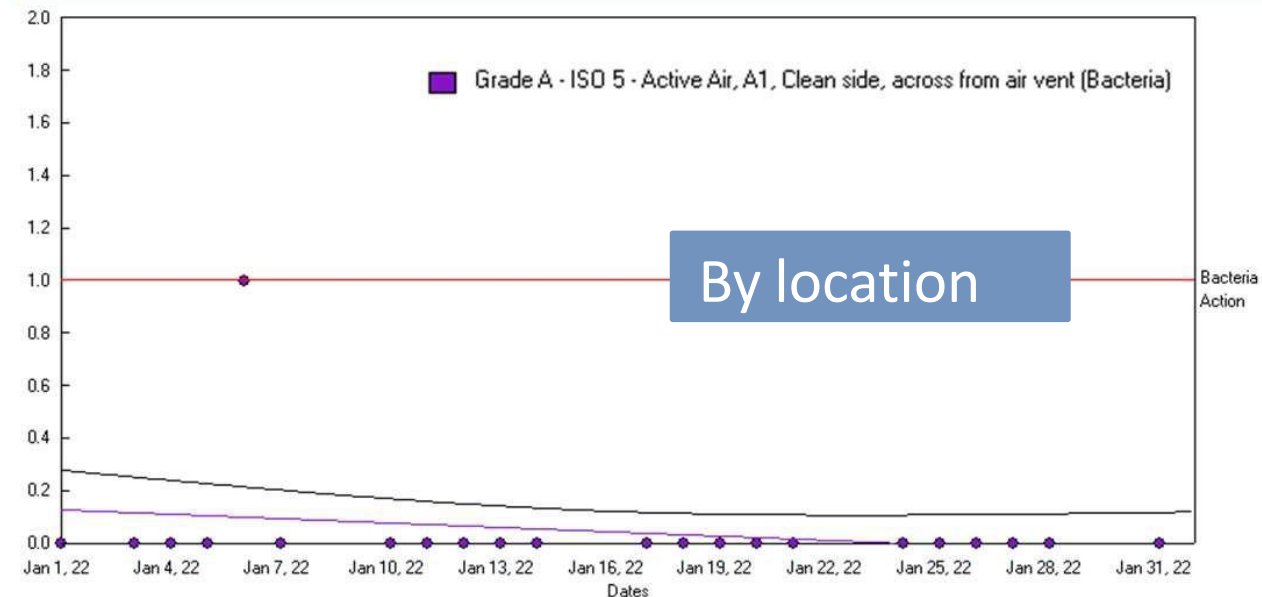
- Preventive trending across all elements
- Routine trending for product release and state of control
- Investigational Trending
- Post Corrective Trending

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Microbial Contamination and Control

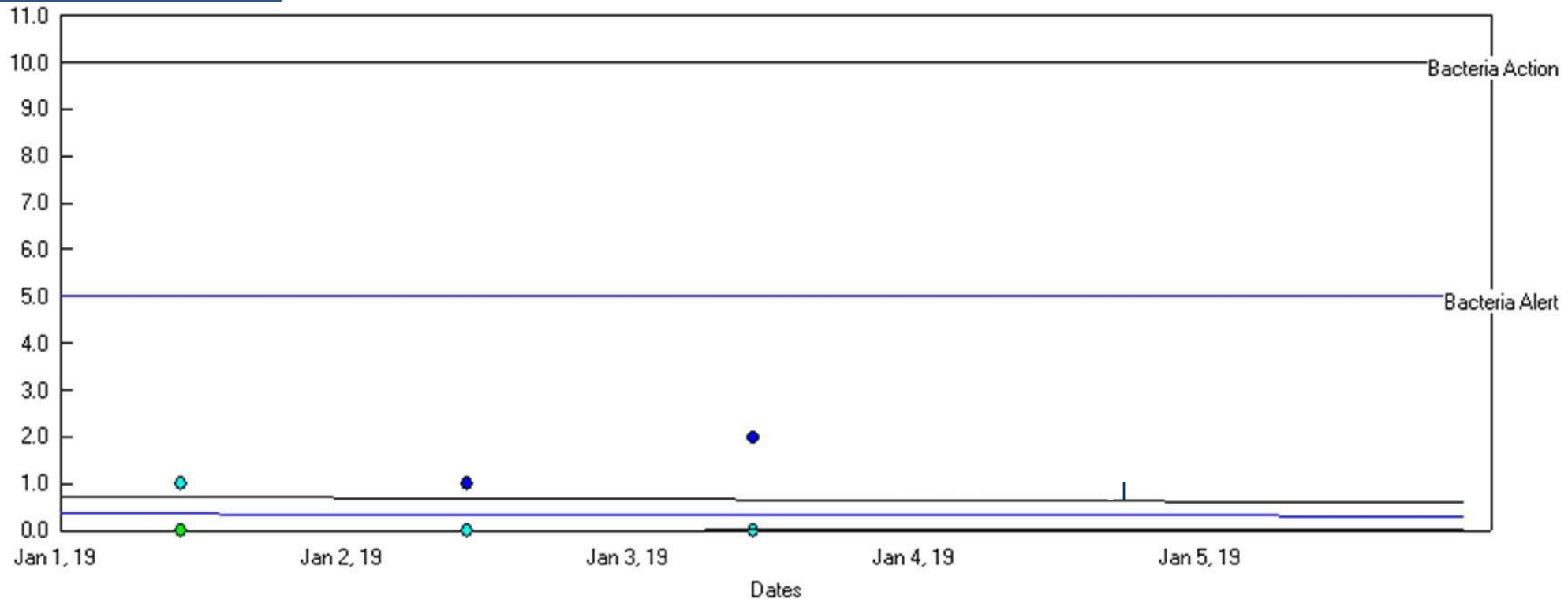
03-04 May
Northbrook, IL





Environmental Monitoring

Within Levels Trending





Environmental Monitoring

Within Levels Trending

Tabular Result Report

Filter: Date test done: Mar 1, 2021-Apr 7, 2022
ID Code: H1 - Room 137
Test Type: Air Sample, Air Sample USP

ID Code	Room	Location	Date test done	Bacteria	Yeast/Mold	Lot Number	Micro-organism ID
H1 - Room 137	Room 137	A1	Mar 2, 2022	0	0	-	-
H1 - Room 137	Room 137	A1	Mar 4, 2022	0	0	lto234	-
H1 - Room 137	Room 137	A1	Mar 9, 2022	0	0	lto234	-
H1 - Room 137	Room 137	A1	Mar 22, 2022	0	0	4233	-
H1 - Room 137	Room 137	A1	Mar 22, 2022	1	0	4233	-
H1 - Room 137	Room 137	A1	Mar 22, 2022	5	0	4233	-

Summary of Tests

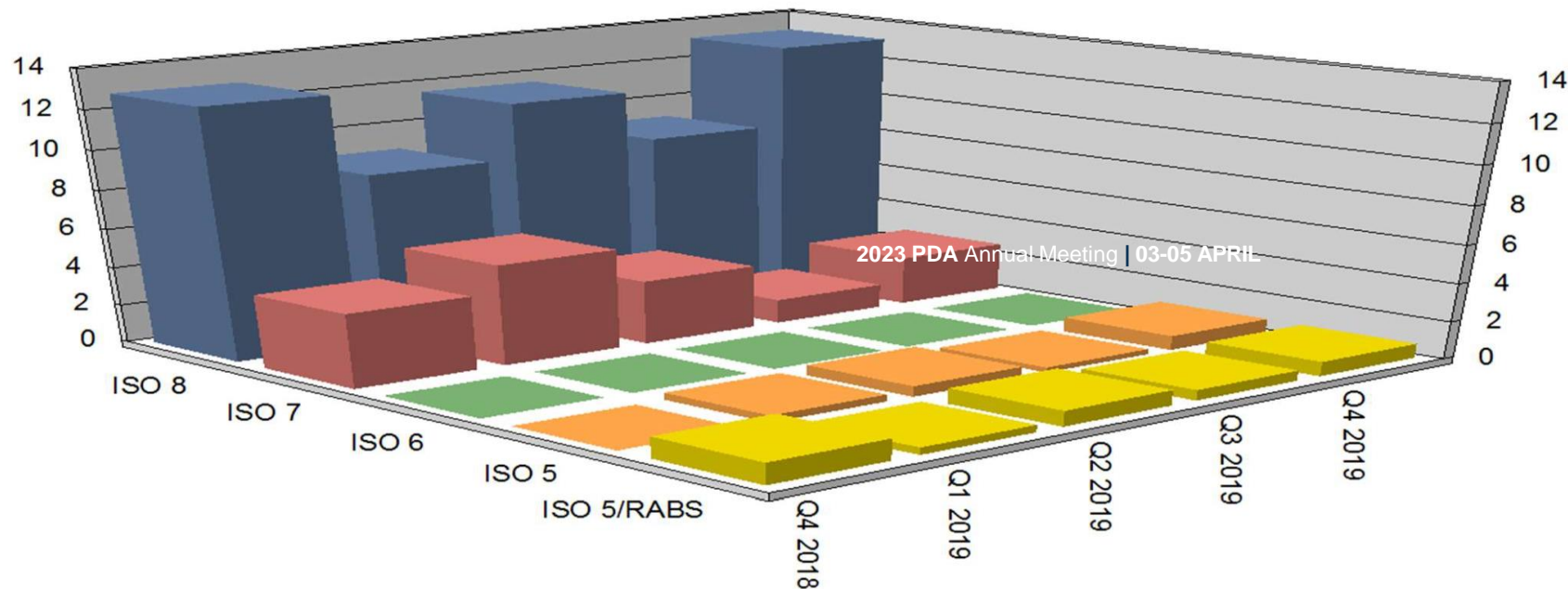
Zeros		Positives		Alerts		Actions		Total Valid Results
Count	%	Count	%	Count	%	Count	%	
4	66.67	2	33.33	0	0.00	0	0.00	6



Environmental Monitoring

Recovery Rate Reporting

Preventive Trending - Q5

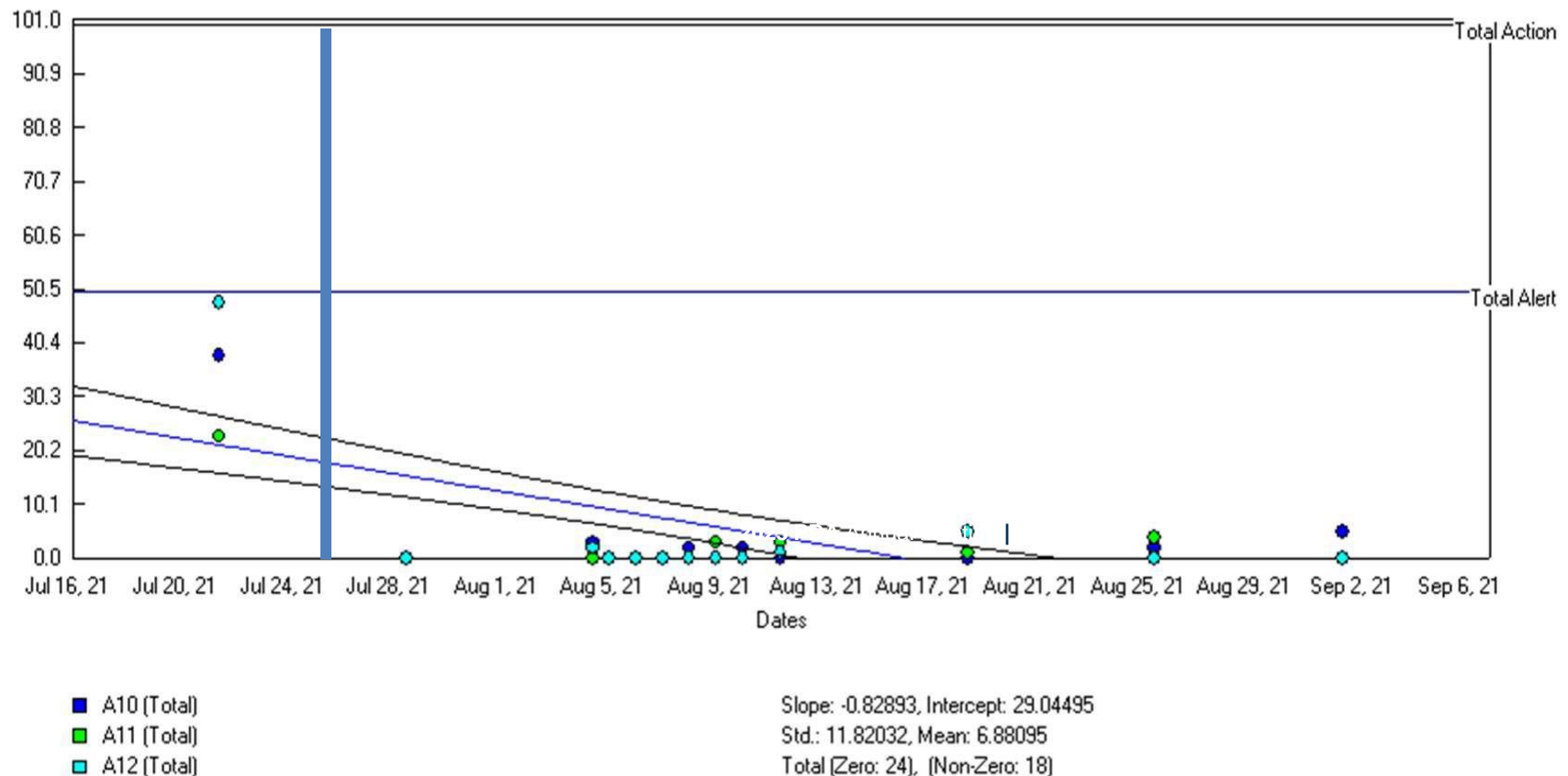




Environmental Monitoring

Post Corrective Trending

Cleaning event





Trending and Data Analysis

- A well-designed, trending program is ***powerful.***
 - CC data must be analyzed; not simply reported
 - What information does the data provide?
 - What conclusions can be drawn?
 - Are new risks identified?
 - Does any action need to be taken?
- Critical and detailed data analysis can greatly facilitate
 - Effectiveness of the CCS
 - Root cause analyses
 - Batch impact assessments
 - Continuous improvement of CCS
 - Continuous improvement of the processes monitored



Manage Digitalization Risks

True Digital Transformation Risk Considerations

- **Data integrity & Compliance risks**
 - Identify all compliance requirements and manage compliance at the workflow step level
 - Consider all ALCOA+ elements as well as corresponding verification and validation activities
- **Cybersecurity risks**
 - Implement robust security measures, such as firewalls, intrusion detection systems, and encryption, as well as training employees on cybersecurity best practices
- **Technical challenges**
- **Cultural challenges**
 - Employees may be resistant to changes in the way they collect, manage, and analyze data, which can impact the success of the digital transformation.
 - Involve employees in the planning and implementation process, providing training and support to ensure they are comfortable with the new system, and communicating the benefits of the digital transformation to build buy-in and support.
- **System Downtime**
 - Perform testing and validation of the new system prior to implementation, as well as having backup systems and contingency plans in place to minimize the impact of any disruptions.
- **Cost**
 - Identify Business Ready Solutions as much as possible
 - Perform cost-benefit analysis to identify potential cost savings and return on investment



Data Integrity Considerations

- **FDA** - Data Integrity and Compliance With Drug CGMP Questions and Answers, Guidance for Industry (*December 2018*)
- **MHRA** - 'GXP' Data Integrity Guidance and Definitions (March 2018)
- **PIC/S** - Good Practices for Data Management and Integrity in Regulated GMP/GDP environments (November 2018)
- **EMA** - Data integrity (August 2016)
- **WHO** – Annex 5: Guidance on good data and record management practices
- **Parenteral Drug Association (PDA)**: Elements of a Code of Conduct for Data Integrity



Planning for Data Integrity Compliance

Workflow step: EM sampling

- Responsible Department: *QC Micro*
- Data Source: *EM Mobile Tablet Solution*
 - Responsible Group: *EM Sampler*
 - Time Spent: *2 min/sample site*
 - *Attributable*
 - *Legible*
 - *Contemporaneous*
 - *Original*
 - *Accurate*
 - *Complete*
 - *Consistent*
 - *Enduring*
 - *Available*



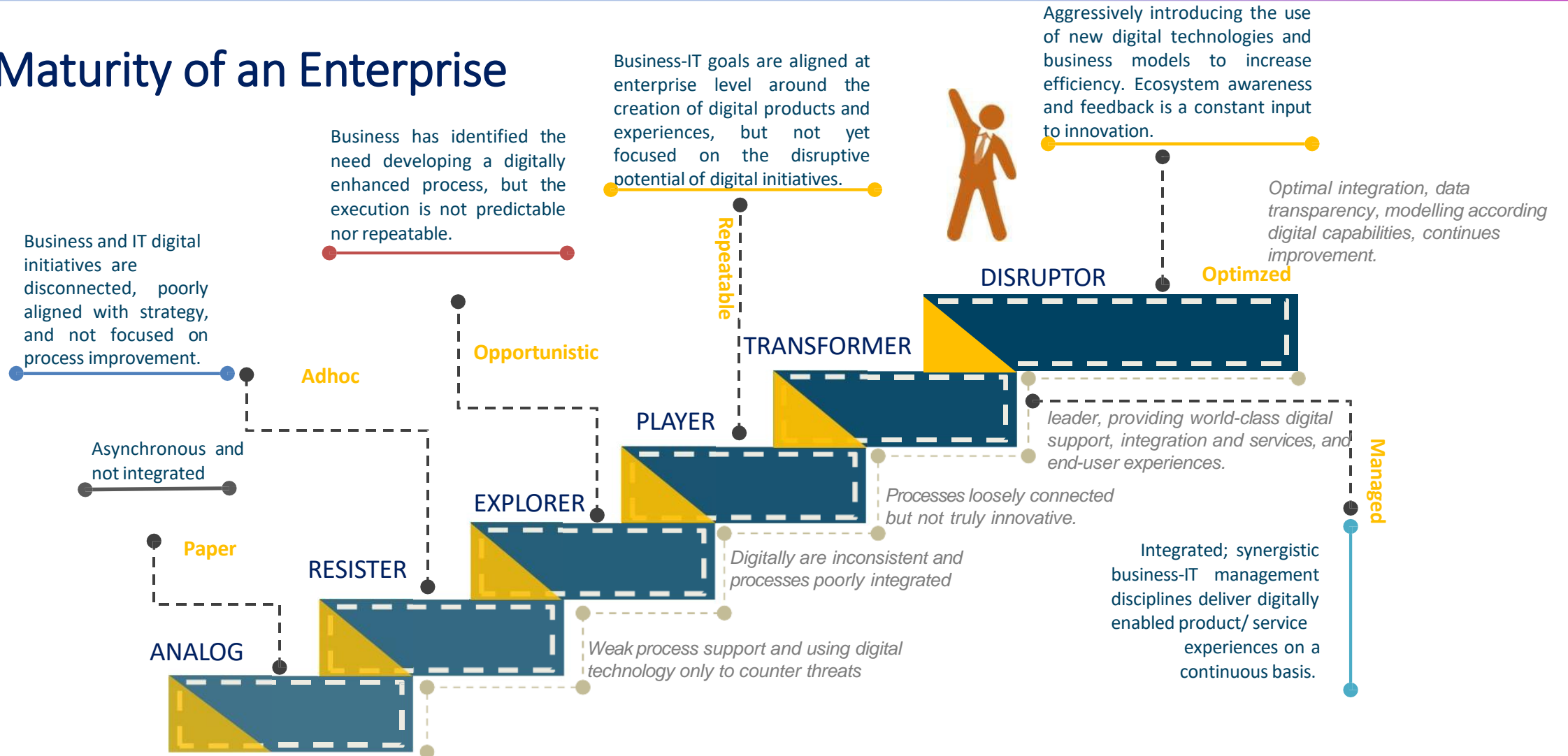
Planning for Data Integrity Compliance

Workflow step: Results Review

- Responsible Department: *QC Micro*
- Data Source: *EM LIMS Solution + Audit Trail Review*
- Responsible Group: *EM Reviewer/Supervisor*
 - Time Spent: *1 min/sample site*
 - *Attributable*
 - *Legible*
 - *Contemporaneous*
 - *Original*
 - *Accurate*
 - *Complete*
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Digital Maturity of an Enterprise

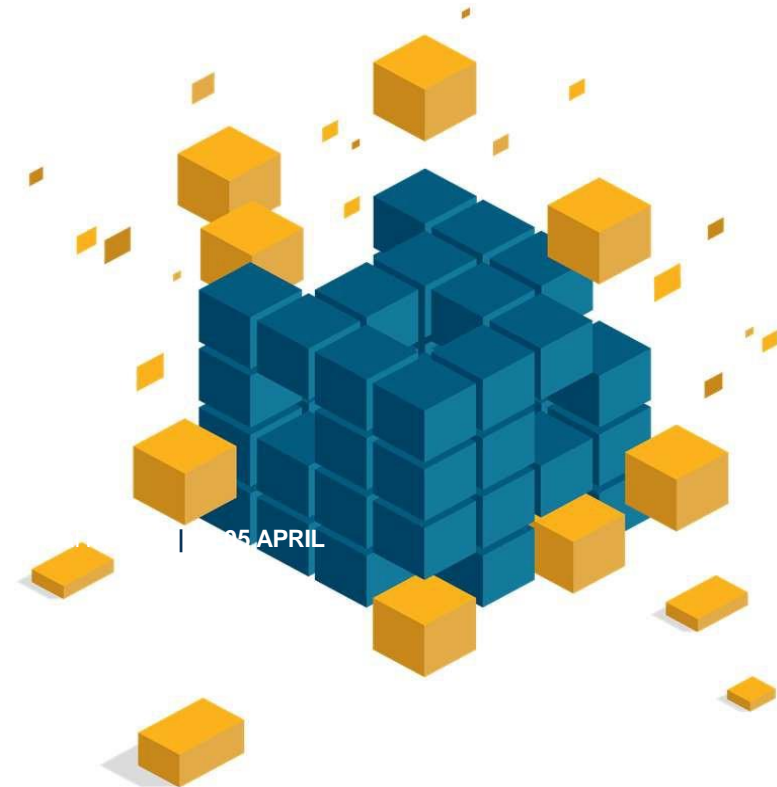




Your data is not just a collection of data !

It's a collection of **built-for purpose information** that supports your operations with value-adding insights, that are to-the-point and accurate.

Built for purpose, “**business ready**” regulatory compliant quality-process management applications should provide holistic, global contamination control analysis.





Thank you!

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Novatek International

Email: Corinne.Cleary@ntint.com

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