DIGITALIZED QUALITY IN LIFE SCIENCES

# Roadmap to Sustainable Growth and Speeding Profitable, High-Quality Products to Market

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*Digitalized Quality in Life Sciences*

# Roadmap to Sustainable Growth and Speeding Profitable, High-Quality Products to Market

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SECTION 1

# Executive Summary

# Yesterday's Quality Systems and Processes Fall Short for Life Sciences Manufacturers

The life sciences industry, and manufacturers that serve this segment, has almost always been in a state of transition. It has such a powerful impact on and connection to public health and therefore spawned increasingly strict regulations from a growing number of regulatory bodies. While there's been some effort to harmonize regulations, the breadth of requirements from a myriad of global regulators continues to add complexity and potential cost across the market. The industry itself along with regulators are also adjusting to growing populations and changing standards of living, global distribution of suppliers and manufacturers, and ever-growing digitalization of products, testing, and distribution.

Medical products, device, pharmaceutical, and other healthcare manufacturers have felt even more pressure in recent years as regulators have emphasized the importance of metrics, quality, and continuous improvement. For example in 2018, the United States Food and Drug Administration (USFDA) released its quality metrics dashboard which clearly displays regulated manufacturers' performance. The agency has future plans to use quality data together with unique device information (UDI) to provide more insight about manufacturer performance, at a level that many manufacturers currently struggle to assess themselves.

# Digitalization is the Way Forward for Life Science Makers

Put simply, the systems and processes life sciences have used to manage quality are now inadequate. However, while current external conditions require manufacturers to adapt and change, they also have a new opportunity to formulate a strategy that creates market differentiation and improves operational and financial performance. The new strategy must align quality with success by design, and transform quality and quality data into a competitive asset. The forward-thinking life sciences enterprise will achieve it by digitalizing data, connecting the digitalized data to related business and operational systems, and applying analytics to identify new insights.

We refer to digitalization of quality across business and operational systems as Quality 4.0. While technology isn't the entire story, Quality 4.0 does require mature traditional quality data and a data-driven enterprise quality management system (EQMS). Furthermore, it builds on and incorporates mature traditional systems, processes, teams, data from other business systems, sensor data from operations and devices, and advanced analytics. Enterprise leaders in discrete, process, and batch industries have leveraged Quality 4.0 to achieve unprecedented insights and performance.

This research report addresses life sciences challenges and how market leaders approach them today. Specifically, it examines:

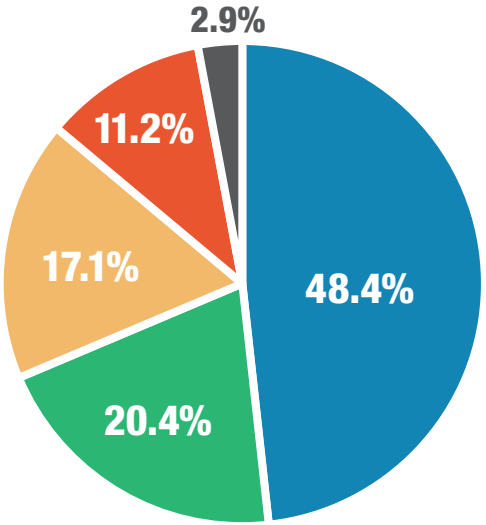
- How rising world populations and standards of living increase spending on healthcare
- Pressures from the USFDA and other regulatory bodies to satisfy cGMP regulations and quality expectations
- Why a shift from traditional quality is necessary to address new expectations and improve corporate success
- How to execute a structured, successful Quality 4.0 journey
- Real-world examples of Quality 4.0 from leading batch and process companies
- Actions life sciences companies can take right now to lay the groundwork for Quality 4.0

SECTION 2

# Research Demographics

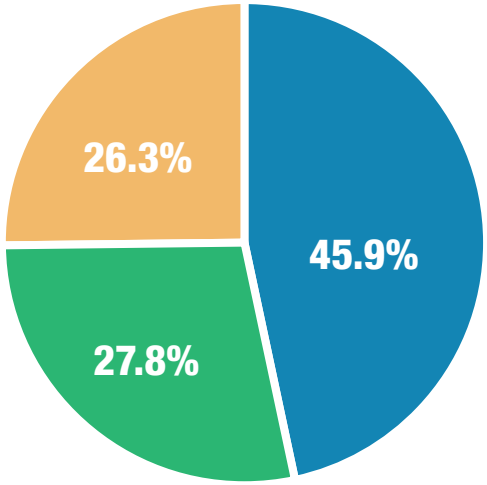
# Research Demographics

For this research we used data from LNS' long-running enterprise quality management system (EQMS) survey, with 1198 respondents. It captures people, process, and technology best practices related to quality, and is a rich source of metrics and KPI data.



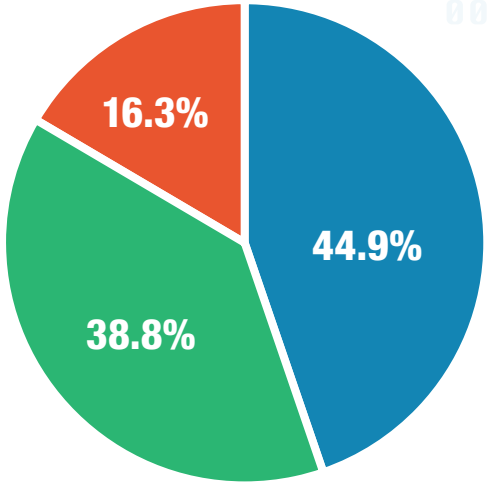

## GEOGRAPHY
COLOR BY HQ LOCATION

- North America
- Middle East and Africa
- Europe
- Asia / Pacific
- Rest of World




## INDUSTRY
COLOR BY INDUSTRY

- Batch
- Discrete
- Process




## REVENUE
COLOR BY COMPANY REVENUE

- Small: $0 - $250M
- Medium: $250M - $1B
- Large: $1B+

SECTION 3

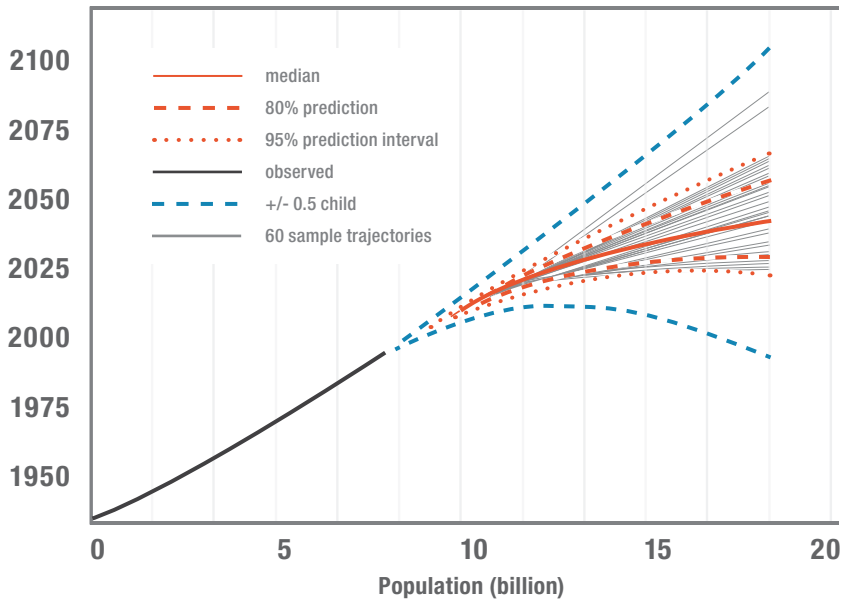
# Life Science Industry Megatrends and Challenges

# Impact of World Population and Economic Growth

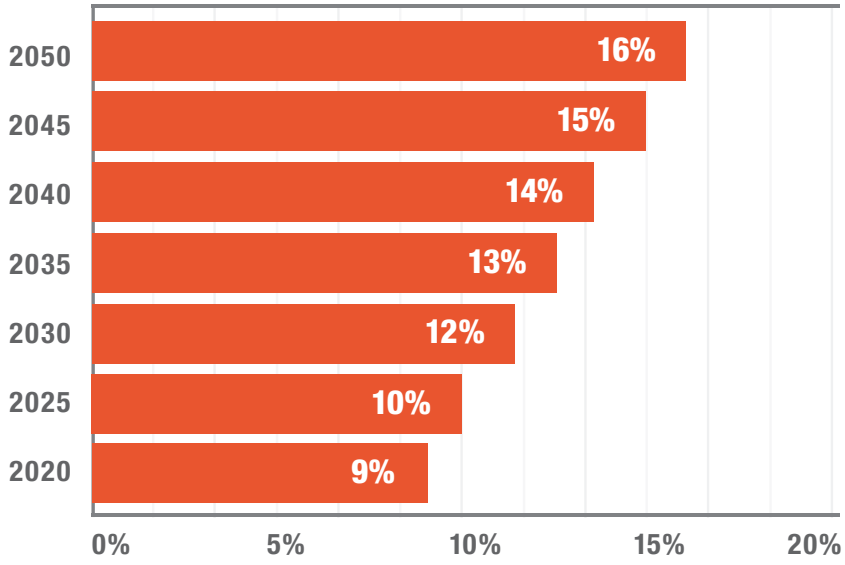
As worldwide population continues to grow and age, the world faces unprecedented challenges in healthcare. In 2017, 8% of the global population was over age 64, and current projections indicate that the number will grow to 16% by 2050. In parallel, the number of high-income households is on the rise, with more than 500 million households earning over $25,000 annually, with over half of the growth in high-income households coming from Asia. As a result, the average increase in global spend on healthcare is expected to rise an average of 5.3% (4.4% per head) annually.[1]

Despite pressure to reduce healthcare costs, market analysts predict sector expansion, driven by advancements in treatment and government initiatives, in response to an aging population and growing incidents of chronic ailments that are expensive to treat.

**World: Total Population**[2]




**Population Over Age 64, % of Total**[3]
**LNS Research Analysis of UN Projections**




[1] *"World Population Prospects The 2017 Revision: Key Findings and Advance Tables" United Nations, Department of Economic and Social Affairs, Population Division, 2017. Accessed June 27, 2018. https://esa.un.org/unpd/wpp/publications/Files/WPP2017_KeyFindings.pdf.*

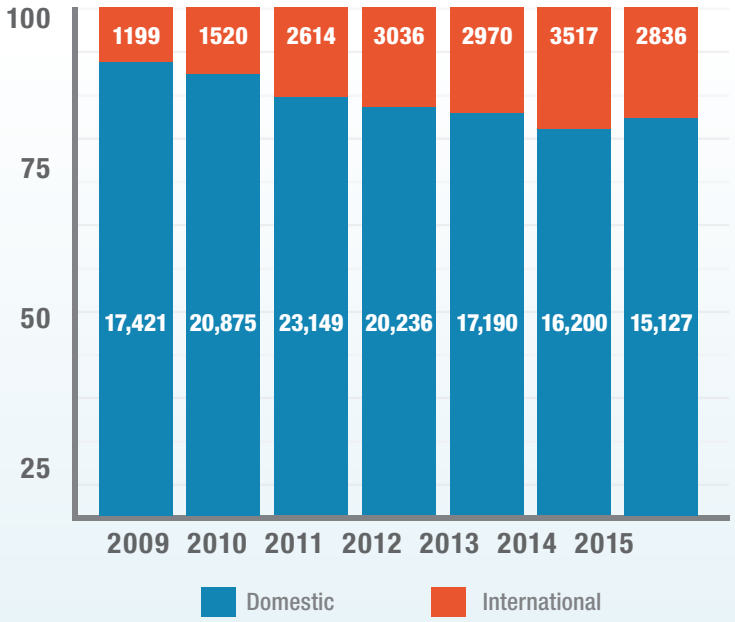
[2,3] *"World Population Prospects Population Division" United Nations. Accessed June 27, 2018. https://esa.un.org/unpd/wpp/Graphs/.*

# Heavy Regulatory Burden for Life Sciences

New challenges have placed and continue to place enormous pressure on life science manufacturers to improve quality management. Regulatory burdens and rising customer demands are two notable examples that have changed the landscape over the past several years and are expected to continue to change the market.

There are many regulatory dynamics underway. The USFDA has taken steps to streamline its approval processes in compliance with the 21st Century Cures Act (Cures Act) and has loosened oversight in areas such as mobile devices. Conversely, it added to the regulatory burden with unique device identifier (UDI) regulations, and invested in data management strategies to quantify and publish quality performance data. The latter possibly created better visibility for the USFDA about makers' performance than the manufacturers themselves. The FDA has also assigned high priority to its Case for Quality initiative, and the market must respond.

**FDA Inspections 2009 through 2015**[1]




Taking a more global view, agencies around the world are generating their own regulatory requirements, which vary by entity. This means high complexity for life sciences companies with worldwide distribution. The total regulatory landscape is increasingly aggressive.

And the complexity just gets more intense as the USFDA places particular focus on the global nature of manufacturing and raw materials sourced from outside the U.S. The number of quality system inspections has generally increased in recent years. From 2005 to 2012, the U.S. FDA's routine Quality Systems Regulations (QSR) inspections increased by a total of 37% and 93% respectively in U.S. and foreign firms.

Forward-thinking companies have already started investing in compliance automation and oversight, and they're using advanced technology to increase quality.

**International inspections increased more than 200%**

[1] *"FDA Inspections 2008 through 2015" United States Food and Drug Administzration. Accessed June 27, 2018. https://www.fda.gov/iceci/inspections/ucm222557.htm.*

# Med Tech, Data and Cybersecurity

Like many industries, life science manufacturers are pushing new limits in product and operational performance with the aid of inexpensive sensors and advances in data connectivity, data storage, data analysis, and data consumption. Innovation in this space is rapid and evolving quickly. More importantly, it can have a significant impact by providing previously unattainable insight into product usage, product transportation, product service, manufacturing equipment performance and operational efficiency, and product quality and reliability. We broadly classify this dramatic shift as Digital Transformation.

The evolution in technology and data creates opportunity for manufacturers to disrupt markets with new offerings, new insights, new efficiencies, and better patient outcomes. However, manufacturers aren't the only organizations experiencing transformation. As previously noted, regulators such as the USFDA are actively pursuing new insights to advance their quality initiatives. Healthcare organizations like hospitals and insurers have their own initiatives too. There's a good chance that non-traditional players might also become disruptive. The January 2018 announcement by Amazon, Berkshire Hathaway, and JP Morgan Chase about forming a new independent company tasked to find new insights, provide transparency, improve outcomes, and reduce the continuously increasing cost of health care is just one example of how new entrants might disrupt the market.

While powerful and disruptive, Digital Transformation increases cybersecurity risk. Life science cybersecurity breaches can be farther-reaching than for other industries, since they can compromise permanent information such as biometric data and health records, and are difficult to overcome. In some cases, data breaches may also compromise patient health.

Technology providers continue to make progress in delivering more robust and secure Industrial Internet of Things (IIoT) platforms that enable disruptive benefits while providing cybersecurity. LNS recommends that manufacturers assess current capabilities against its definition of IIoT platform.

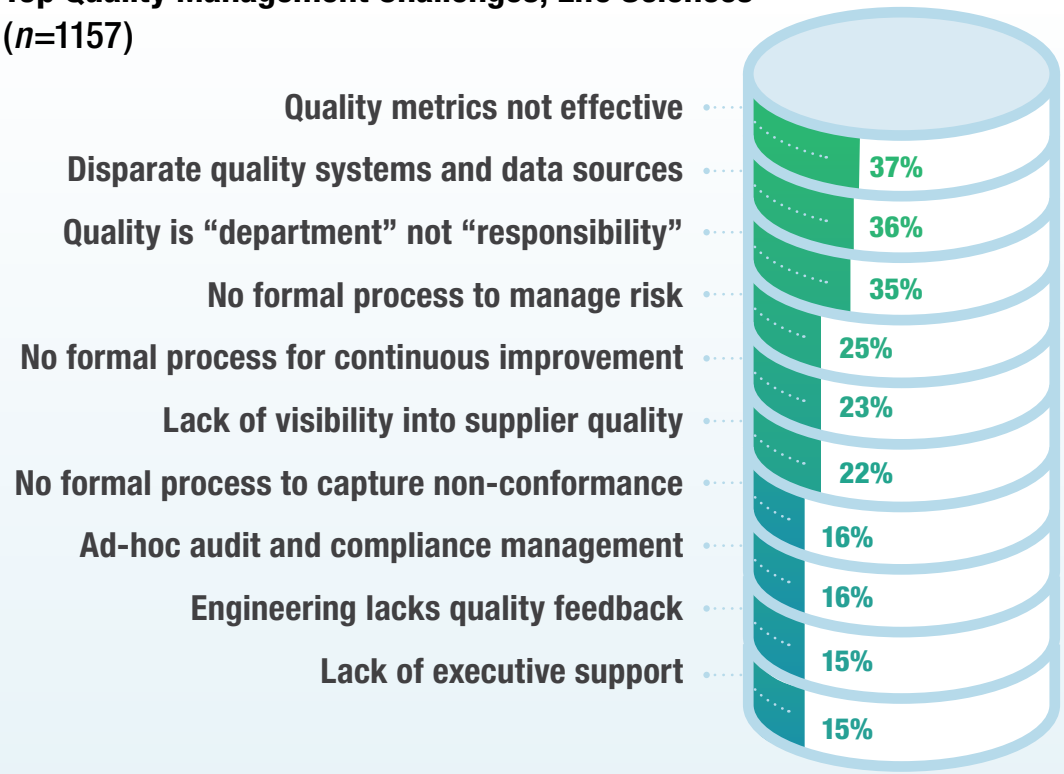
**INDUSTRIAL INTERNET OF THINGS PLATFORM**
by LNS Research describes the connectivity, network styles, and applications framework to support smart connected operations and smart connected assets; within and across a plant, facility or production network in a manufacturing or other industrial operations setting.

*Click to learn more about the* **Industrial Internet of Things Platform**

## Also Trending Now: Quality Management Challenges

The quality management survey by LNS Research brings into focus the roadblocks standing between life sciences manufacturers and effective quality management. When asked about top challenges, executives from all life sciences sectors placed considerable emphasis on culture of quality, effective quality metrics, and disparate systems and data sources. Also, more in-depth analysis shows that pharmaceutical manufacturing companies in particular struggle with visibility into supplier quality. This deficiency is especially relevant today as the USFDA and other international regulatory bodies investigate new technologies such as blockchain to track supplied materials safety.

### Top Quality Management Challenges, Life Sciences (*n*=1157)



# Top Pressures According to Life Science Manufacturers

LNS Research asked life sciences executives specifically about top trends that impact the organization. Not surprisingly, two-thirds cited regulatory requirements for quality management as having the biggest impact. Not far behind were concerns about the ability to connect quality across development and process. These challenges underscore the importance of solving top quality management objective gaps in quality metrics, disparate quality systems, fragmented data, and cultural silos.

Manufacturers must reexamine their strategies for quality and compliance data management, analytics, and consumption to improve efficiency and outcomes. These challenges highlight the need for total quality and compliance technology in life sciences, to provide insights and collaboration while ensuring compliance.

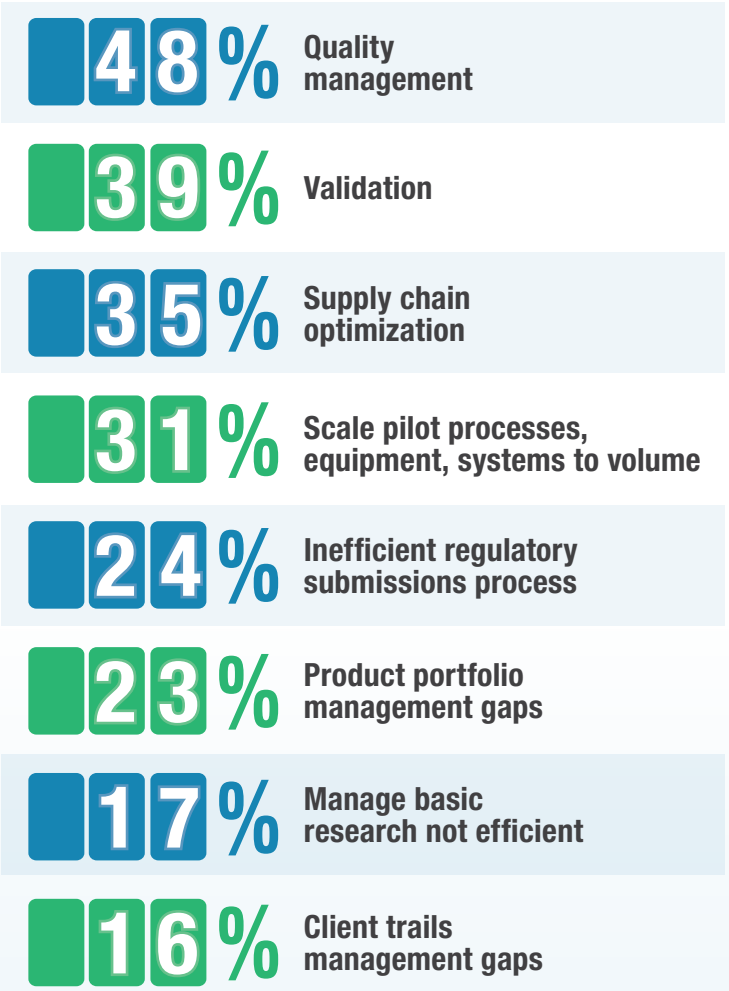
## Top Pressures, Life Sciences

# Quality Management #1 Roadblock to NPI, Speeding Products to Market

It's no secret that new product introduction (NPI) drives revenue spikes, and therefore speeding new products to market has a significant impact on corporate performance. The importance of time to market has increased in life sciences because of the market megatrends examined previously. Forward-thinking life science manufacturers must bring new, innovative products to market quickly to capitalize on intellectual property and current market conditions. LNS tracks the top challenges in time to market, and we're astonished to learn that while regulatory submissions process, clinical trials, and scaling pilot processes to volume play an essential role, they're not executives' top concern.

The number one challenge life science manufacturers face in speeding products to market is quality management, with nearly half the market raising this as the top issue. In context of industry megatrends and other life science challenges, this deficiency underscores the importance of a new approach to quality. LNS recommends that life science manufacturers closely couple quality with the product development process, centralize and harmonize core quality processes and data, and leverage digitalized quality data to drive new insights about operations and new product introduction.

## Top Roadblocks to NPI and Speeding Products to Market, Life Sciences



SECTION 4

# What is Quality 4.0?

# Giving Quality Perceptions and Approaches a Facelift

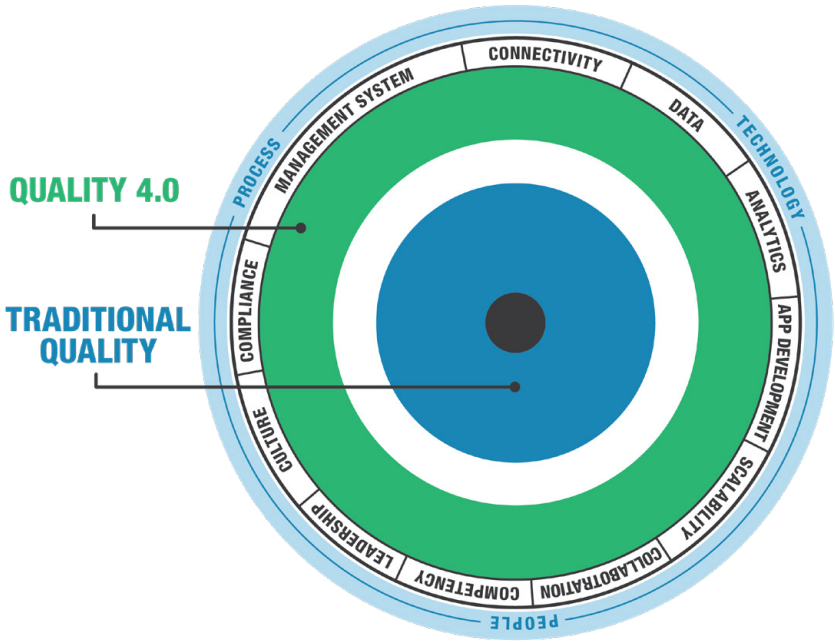
Quality 4.0 is the digitalization of quality. It has been brought about by a long list of technology advances across several areas that together enable innovation, new insights, connectivity between people, and connectivity between people and machines. Just a few examples from a long list include:

- **SENSORS** | Today's inexpensive, highly capable sensors have made it possible to capture more data about device performance. Devices may be manufacturing machines, test equipment, transportation, consumer goods, or wearable technologies.
- **INTERNET** | Social media and online marketplaces have created new collaboration paradigms, and now drive "5-star" quality targets for some manufacturers.
- **BIG DATA** | Data from sensors combined with data from social media, video, traditional business systems, traditional operational systems, and other sources can be streamed back to a centralized database, creating massive quantities of data called Big Data.
- **ANALYTICS** | Machine learning (ML) and artificial intelligence (AI) are analytical technologies that scour Big Data and traditional data to reveal previously unknown patterns. Traditional metrics might show the number of audit findings, identify cycle times for non-conformances and corrective actions, or analyze the standard deviation of parameters. ML/AI creates new, highly meaningful insights. It analyzes data and determines outliers which can be used to issue alerts, predict future events (predictive analytics), or even autonomously make decisions (prescriptive analytics). ML/AI enables zero defect initiatives by discovering new correlations between manufacturing data and customer complaints or warranty claims. These correlations allow manufacturers to form accurate predictions and act in real-time to reduce in-service issues.

Quality 4.0 builds upon traditional quality and requires a solid foundation of traditional quality, manufacturing, and service people, processes, and technology. Manufacturers that want to take a deeper dive into Quality 4.0 should read the definitive ebook on the topic.

**QUALITY 4.0** by LNS Research describes how manufacturers use modern technologies such as advanced analytics and digital connectivity to transform traditional quality and improve operational excellence; enabling enterprise efficiencies, innovation, performance, or strategic objectives.

*Click to learn more about the* **Quality 4.0 Framework**

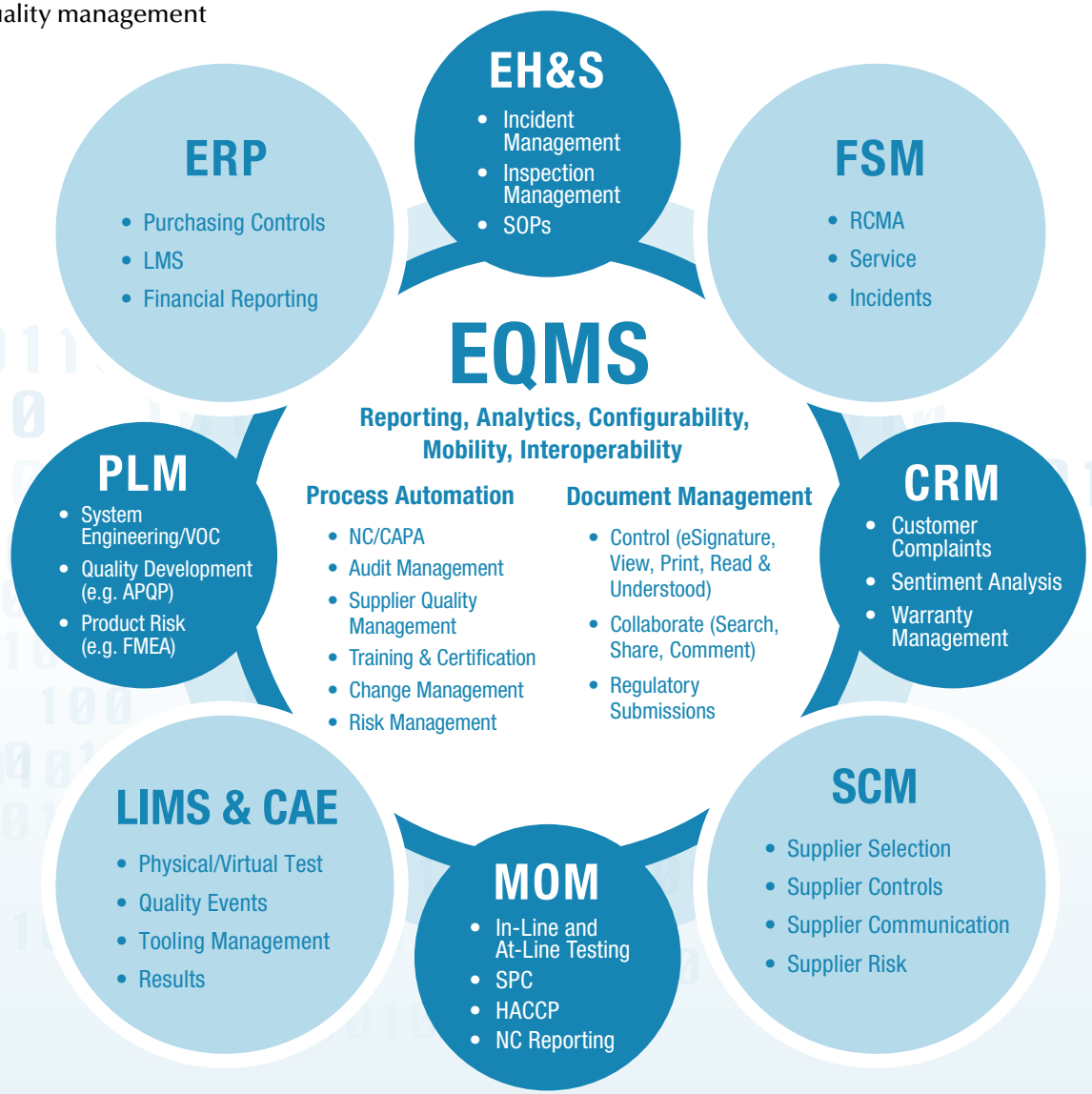


SECTION 5

# Shoring Up Traditional Quality

## Set Priorities Based on Strategic Objectives and Desired Outcomes

Traditional quality is the collection of competencies, compliance approaches, processes, connectivity, data, analytics, and collaboration that pre-dated Industry 4.0 and Digital Transformation. From a technology perspective, these include traditional information technology (IT) systems and traditional operational technology (OT) systems. Examples of traditional IT are enterprise quality management system (EQMS), enterprise resource planning (ERP), customer relationship management (CRM), and product lifecycle management (PLM). Traditional OT systems include manufacturing operations management (MOM), data historians, statistical process control (SPC), and industrial automation.




## Set Priorities Based on Strategic Objectives and Desired Outcomes *(Cont.)*



While Digital Transformation can change the roles of these systems, the data contained within them is if anything more critical for Quality 4.0. It's the foundation that provides context for sensor data and valuable inputs into ML/AI.

Quality data in particular has been highly fragmented, as noted previously. Companies have spread quality processes across the lifecycle and departments, and as such, quality data is often spread across multiple systems and a plethora of spreadsheets, electronic documents, and emails. Companies that have made the investments needed to harmonize these processes and centralize quality data and analytics are well positioned to expand on their investment with Quality 4.0.

Companies that have not must first shore up their traditional quality process and data landscape. LNS recommends prioritizing this journey based on Strategic Objectives and desired outcomes.

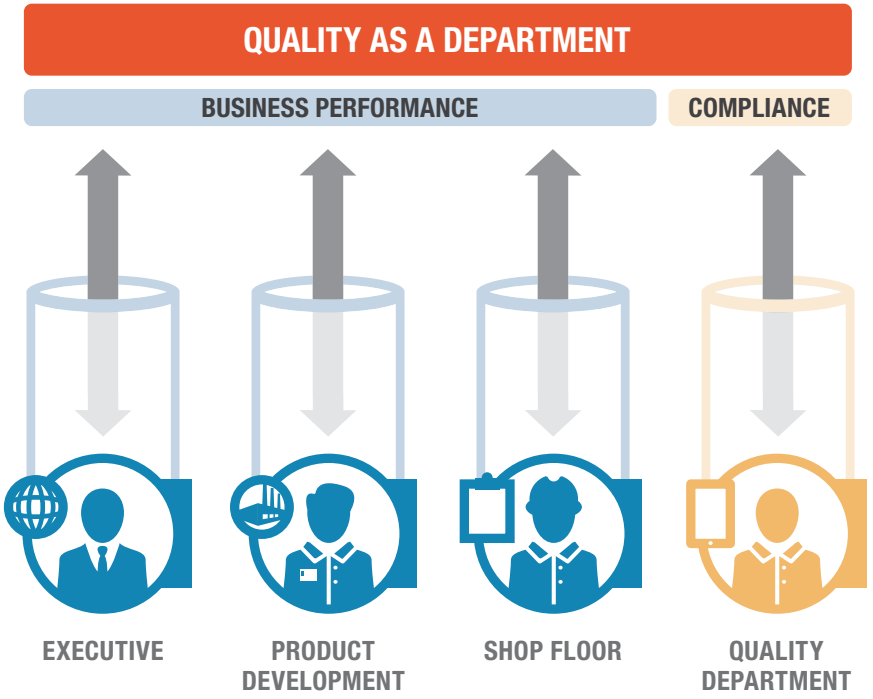
SECTION 6

# The Road to Quality 4.0

## "Quality is a Department" is a Serious Disadvantage

While technology enables Quality 4.0, the impact truly encompasses people and process as well. An effective quality strategy must foster a culture of quality. Like all areas of business, leadership and culture experience a similar set of maturity phases that progress over time. When it comes to quality and compliance maturity in life science manufacturing, a culture of quality is virtually non-existent early on. There tends to be a disconnect, and "quality" is considered a department rather than a responsibility. As we illustrated in the previous section, survey data shows that more than one-third of life sciences organizations have this kind of mindset. This is the source of many other challenges because of high quality and compliance requirements for life sciences.

Although many organizations suffer from "quality as a department" mindset, in many ways it also puts them at a serious disadvantage. When the people throughout the company perceive quality this way, the enterprise is more likely to deal with issues reactively, employees tend to view quality as a policing function, and quality outside of the manufacturing environment is difficult to manage. Companies more effectively manage quality when they shift resources toward proactive measures; this rings true whether discussing people, processes, or technology.



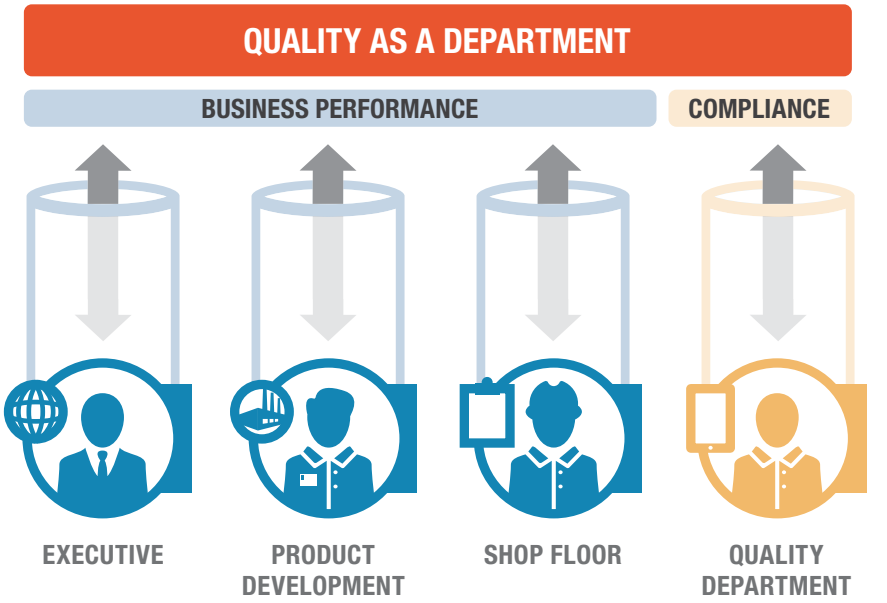

**1 in 2** executives stated their organization considered quality more of a department than a responsibility.

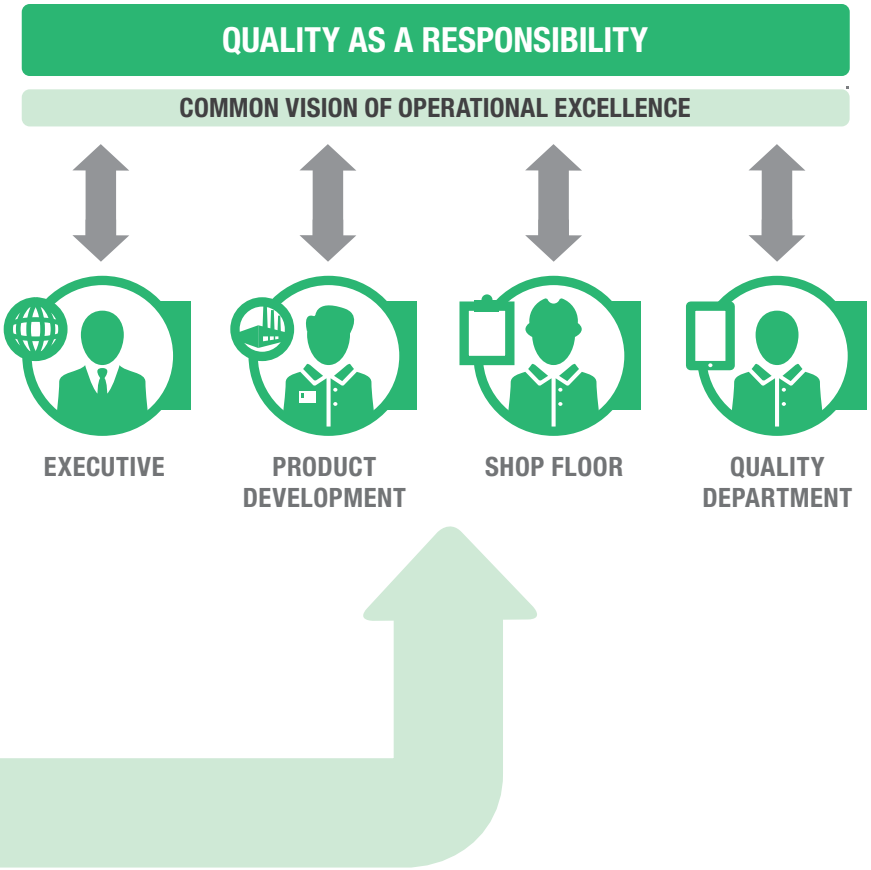
## Inspire "Quality is a Responsibility" Thinking

Changes in perception about quality are possible, but they occur much more quickly when sponsored by corporate leadership. In fact, executive sponsorship for quality is the single most significant difference between more mature and less mature organizations. Research by LNS shows that companies with top-level support have adopted 2.7 times more quality management best practices on average than those without it. Bringing together research and development, operations, and quality makes a big difference. Too often however, grassroots campaigns fall by the wayside because workers don't take them seriously. To gain momentum and drive transformation, LNS Research suggests that executive leaders incorporate quality and compliance in the Operational Excellence strategy.

LNS Research also recommends that quality leadership clearly demonstrate the connection between quality and the ability to achieve Strategic Objectives and corporate objectives. What's more, they should establish the link between quality and the goals and initiatives of peers in functional areas like product development and manufacturing operations. Quality leadership must employ a strategy for improvement that spans the eleven elements of Quality 4.0, and explicitly align the Quality 4.0 strategy and journey to corporate and cross-functional success.

The combined actions of quality leadership and executive management drives a progression toward quality as a responsibility. While it happens organically, there are several things executives can do to accelerate momentum.



# Harmonize Quality Processes and Data

Like many industries, life science manufacturers continue to experience continued mergers and acquisitions (M&A). One typical result of M&A activity is fragmented processes, competencies, and technologies across the formerly separate corporate entities. In light of the already siloed quality landscape, this common scenario creates a significant quality data challenge which companies must overcome to make progress toward Quality 4.0.

LNS Research recommends that organizations flexibly unify (harmonize) quality processes and data across the firm, within formerly separate quality teams and across related functions. Those taking on this challenge must address several goals. They should:

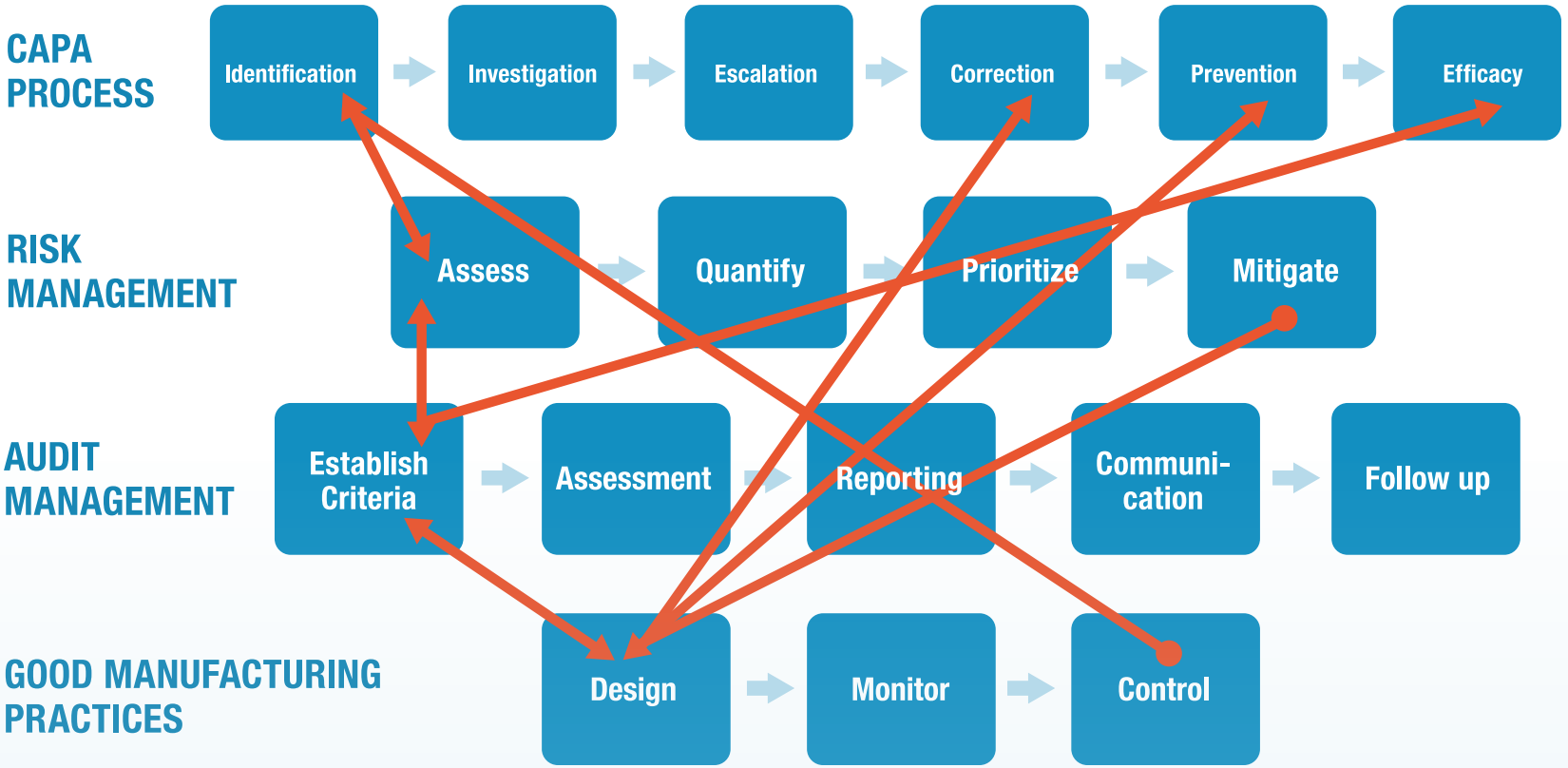
- Share data with all internal stakeholders in support of cultural initiatives and transparency in quality performance;
- Establish the right metrics and key performance indicators (KPIs) to support data-driven decisions by extended teams; and
- Shift quality away from its current document-centric posture to a more powerful data-centric approach, which provides a critical and centralized data source for IIoT/Quality 4.0 initiatives.

**Executives responsible for quality can help the enterprise make progress by doing the following:**

- Third-party quality audits
- Assess and prioritize areas of improvement based on internal and third-party quality audits
- Create a corporate communications plan to engage the workforce
- Develop a short and long-term plan for internal education, process improvements, and capital investments
- Require managers to regularly review performance and plan for improvements
- Establish performance-based programs and rewards based on quality metrics
- Stay current on quality trends, emerging technologies, and regulations
- Develop a resource center with dynamic quality education courses, SOPs, and instructions
- Drive operations performance with quality metrics such as cost of quality (CoQ)

# Harmonize Quality Processes and Data *(Cont.)*

## Quality Too Valuable to Reside in Silos

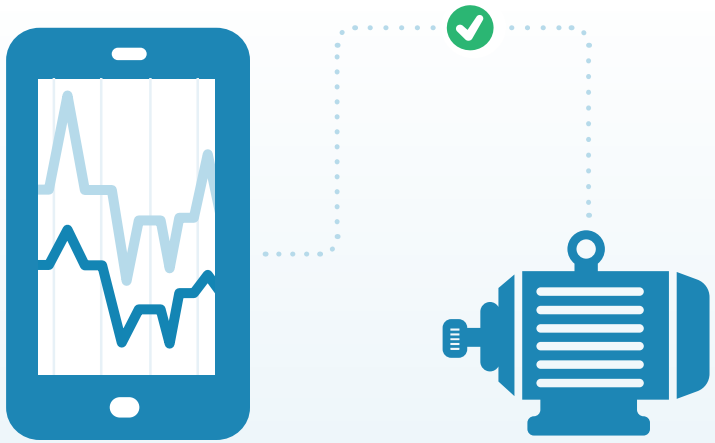


# Connect Quality Management and Quality Execution

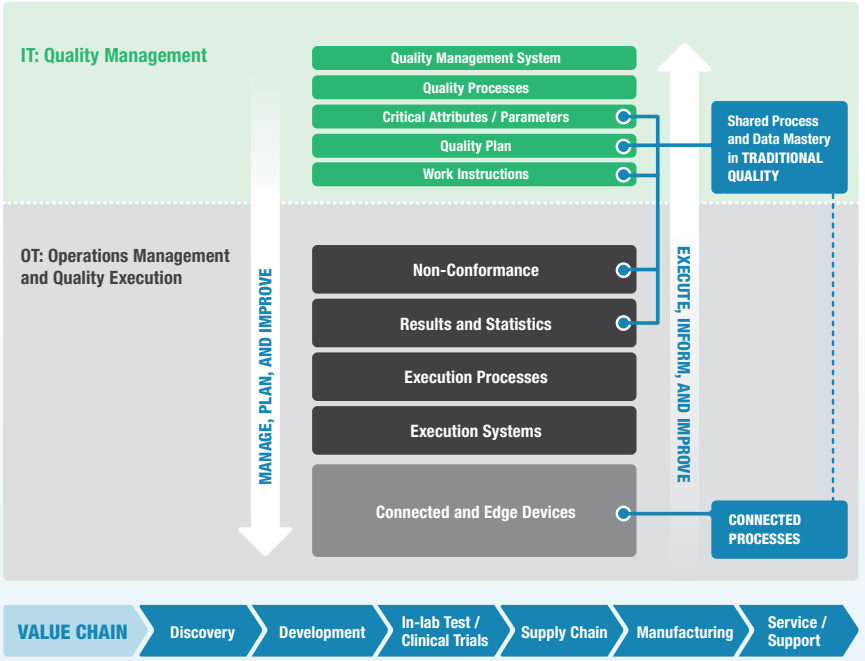
There is a pronounced disconnect between the execution of quality activities in operations, and quality management, as LNS revealed earlier. Companies that have executed LNS' recommendations related to culture, processes, and data are well-positioned to connect these and drive game-changing operational and financial performance.

Life science manufacturing firms can leverage the Quality 4.0 technologies discussed earlier to capture unprecedented insights about operational performance. They can compare insights gained from execution to quality management expectations and plans set during product development and production planning to arrive at lessons learned, improve future predictions, and drive necessary corrective actions.

LNS Research is tracking the progress of many Quality 4.0 use cases across industries. Innovation leaders are applying Quality 4.0 technologies to generate fresh insights during clinical trials, new product testing, production planning, manufacturing operations, product distribution, and service. We selected the following use cases to demonstrate just a few of the many possibilities to improve operational and financial outcomes.



## IT/OT CONVERGENCE



SECTION 7

# Quality 4.0 Use Cases

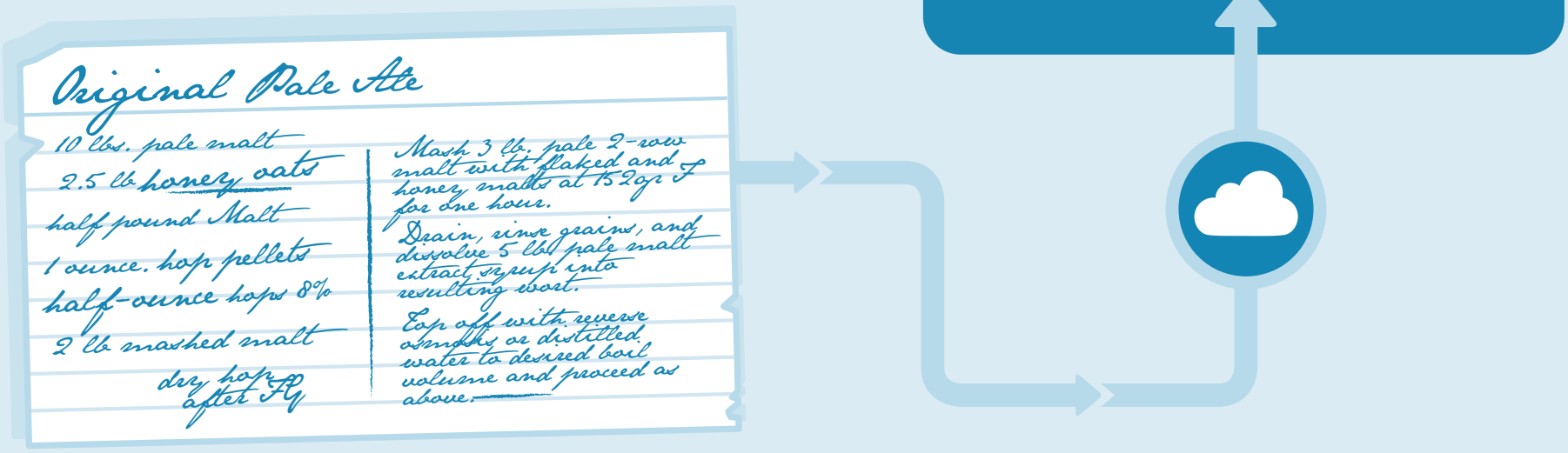
# USE CASE 1: Managing Recipe Variation

Anyone that has ever home brewed beer knows it can be a touchy process, fraught with seemingly mysterious relationships between live cultures, bacteria, time, temperature, ingredients, equipment, elevation, and much more.

Given all the possible sources of variation in recipes, sometimes even top brewmasters can make mistakes. One of the largest craft brewers in the US recently engaged in an IIoT project using ML/AI and historical process data to solve a batching problem that was resulting in a major quality issue and the loss of entire batches.

The brewmasters thought the problem was the relationship between pressure and temperature; it turned out to be an issue with the timing of batch processes determined by natural variances in yeast. Using ML/AI the brewmasters built a model to alter the recipe and optimize batches on previously unknown relationships.

With the new process established, they eliminated lost batches for this quality issue and recaptured two weeks of extra capacity per lost batch.

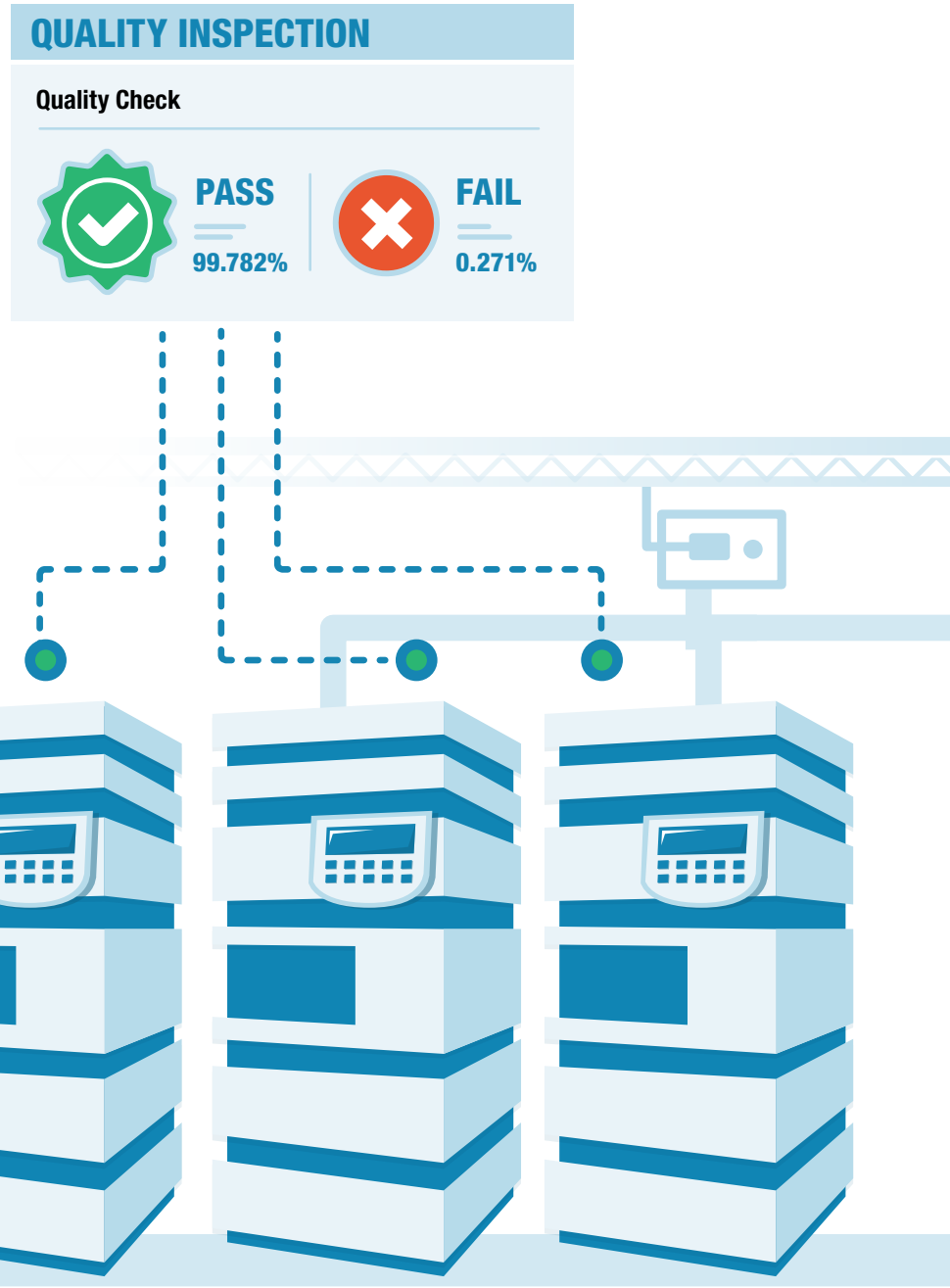


# USE CASE 2: Disruptive Quality Testing

Quality testing and validation comes at a cost and is often a significant contributor to the total cost of quality incurred by a company. Because of these costs, quality best practices dictate that instead of testing every finished product, industrial companies should monitor the production process itself. They test the capabilities of a process and then assume if the process stays within controls limits the finished product stays within specification. Furthermore, they reduce finished product testing to a small fraction of total production just as a failsafe. Of course, no system is foolproof, and anything short of 100% finished product testing can still result in quality issues making it to the field.

As with other areas of operations, the IIoT and smart connected assets are changing this game. Connected manufacturing assets provide continuous digital data that is increasingly gathered and analyzed with Edge devices. This enables continuous testing throughout the manufacturing process, which exponentially reduces variation and increases product conformance. Conversely, when end-products have intelligence and connectivity built in, there are opportunities to use these capabilities to dramatically reduce the cost of quality testing and in fact, build quality testing into the production process.

LNS Research is aware of at least one leading smart connected products company that is using new connectivity and intelligence capabilities in the end product to conduct quality testing during production and eliminate previously undetected dead on arrival (DoA) failures from reaching the customer's doorstep.



# USE CASE 3: Managing Customer Complaints

Customer complaint management is a critical quality input, providing both positive and negative lessons learned. Complaints are a leading indicator of customer purchasing behavior and can also influence the market, particularly in consumer-facing products. Quality 4.0 has sparked innovations in customer complaint management in business-to-business (B2B) and business-to-consumer (B2C) settings.

LNS Research is aware of several companies that leverage augmented reality and smart devices to gather more information during B2B customer complaints. Using augmented reality devices, manufacturers have been able to inquire and receive additional information real-time, virtually. The faster pace of information has led to quicker root cause diagnosis and issue remediation.

A leading automation equipment supplier deployed a somewhat different B2B approach. Low-frequency, random failures plagued the vendor and caused expensive line outages. The result was low volume and very high severity customer complaints; both were threats to the business line. By adding sensors to its equipment and applying machine learning analytics, the manufacturer found that it could correctly identify failures, predict when failures would occur, and perform maintenance during scheduled downtime.

Social media is a new and important customer complaint data feed with significant implications for manufacturers of over the counter (OTC) regulated goods. Trending social media topics can quickly promote a brand or almost instantly cause irrevocable damage by shaping the market's perception. Many consumer products companies use “social listening” technologies to track consumer comments on social media and other Internet venues. These strategies include the ability to convert social data to customer complaints, which the company can then automatically route to appropriate parties, track and remediate.

SECTION 8

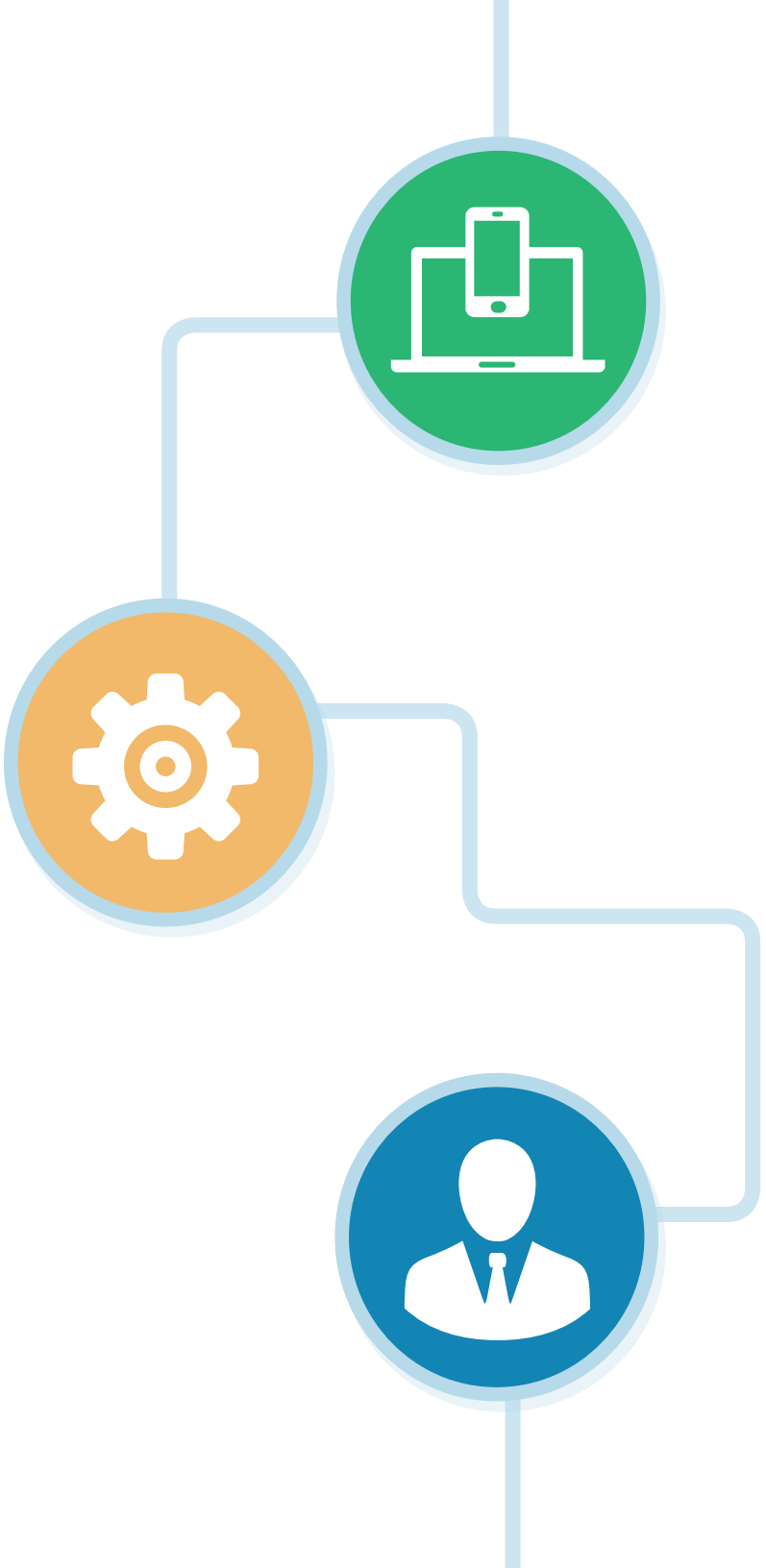
# Takeaways and Recommendations

## Takeaways

Although yesterday's quality systems and processes fall short for life sciences manufacturers, there is a clear way forward with Quality 4.0. Digitalization – broadly termed Digital Transformation, can align people, processes, and technology to overcome market pressures and their own deficiencies, to transform quality and quality data into a competitive asset. Savvy life sciences makers will understand that Quality 4.0 isn't just about "software." Instead it builds on and incorporates mature traditional systems, processes, teams, data, and advanced analytics to achieve unprecedented insights and performance. Companies eager to embark on a Quality 4.0 journey should prepare themselves in the right focus areas:

- **Understand life sciences trends and drivers.** The life sciences market continues to face macroeconomic and global population trends, regulatory changes, and rapid evolution of technology and data science. These conditions present new opportunities, and simultaneously increase pressure on new product introduction and production, both of which can have a negative impact on delivered quality. Tomorrow's market leaders will adapt to these pressures now to continuously improve quality.

- **Build a culture of quality, with a top-down approach.** Top management and quality leaders must align the quality strategy with corporate Strategic Objectives, leading the way to instill a culture of collaboration where the organization incorporates quality and compliance initiatives into all areas of the value chain, rather than quality being seen as a "policing function."



## Takeaways *(Cont.)*

- **Lead with quality data.** Market forces tend to further fragment an already siloed quality process and data landscape. Forward-thinking businesses should take a platform approach to EQMS, breaking down informational silos, connecting quality data across the corporation, and enabling all functions to play their role in leading with data-driven quality decisions.
- **Digitally transform quality management and execution.** Disconnected quality management and quality execution is a leading challenge for the market. Innovation leaders have already adopted advanced technologies like sensors, collaboration tech, data management, and analytics to drive new operational insights and translate these insights into tactical and strategic advantages.

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