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REPORT

# The Current Pharmaceutical Quality Landscape

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In recognition of Quality Week, this compilation contains four recent articles on the current state of pharma quality:

- Pharma Must Develop Quality Leaders: Here is One Approach
- How to Assess and Advance a Pharma Company's Quality Maturity
- Synergy at the Intersection of Data Integrity and Quality Culture
- Ashley Boam on FDA's Proposed Quality Maturity Model

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## ABOUT THE EXPERT



**Jerry Chapman** is a Senior GMP Quality Expert at Redica Systems. He brings 40 years' experience in the pharma industry, including 31 years at Eli Lilly in technical and leadership positions in research and product development, manufacturing, plant quality, site quality, corporate quality, and quality systems.

## PHARMA MUST DEVELOP QUALITY LEADERS: HERE IS ONE APPROACH

Unlike in business or engineering or medicine, advanced degrees and training in the science of manufacturing quality are not available. Yet product quality is of fundamental importance to drug companies, their patients, and the institutions that regulate them.

Efforts in the past few years by a team of chief quality officers resulted in the development of an undergraduate minor in quality to accompany a college-level science major, an important effort that provides relevant training to entry-level quality professionals. But education in the science and art of quality assurance is still needed for company leaders and executives.

AstraZeneca recently shared a comprehensive program it has established for the training and development of quality leaders, which it calls “The Modern Quality Professional (MQP) Development Tool.” At the 2021 PDA Annual Meeting held virtually in March, AstraZeneca Product Quality Group Head Stephan Krause presented the MQP tool his company developed. The tool is being used to provide a development

pathway for AstraZeneca’s quality professionals and specifically its Product Quality Leader (PQL) role.

He shared a quote from AstraZeneca Global Quality Head Anthony Mire-Sluis, commenting on the importance of the MQP effort. Mire-Sluis said, “the necessity to move from the traditional concept of a compliance/checking mindset to one where we partner with the business using science and risk along with appropriate communication and leadership skills is essential to having quality built in and a quality culture

The tool is being used to provide a development pathway for AstraZeneca’s quality professionals and specifically its Product Quality Leader (PQL) role.

throughout operations. The MQP program has not only identified the capabilities necessary but provides the relevant training and experience to achieve its aims.”

Krause also provided the company vision for the role.

“The MQP is scientific, courageous, accountable, partnering and delivering,” he said. “These attributes of the MQP can also be

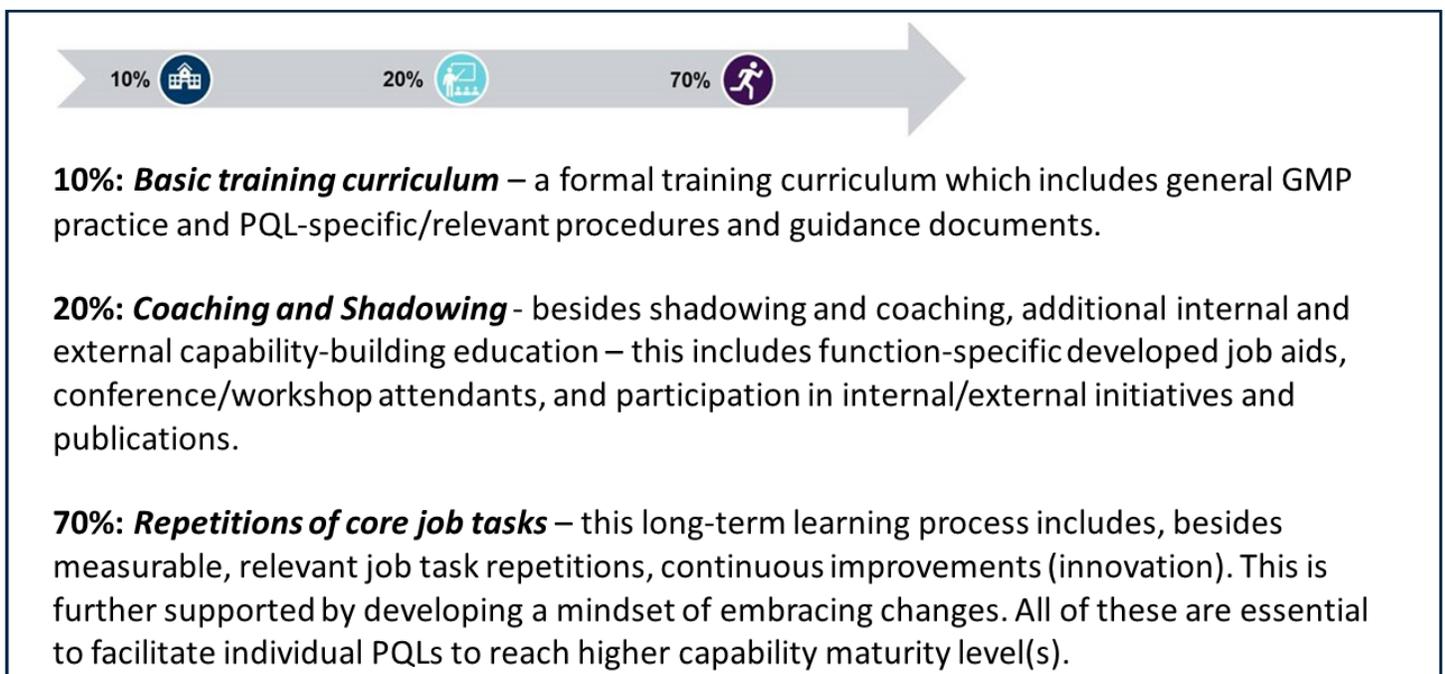
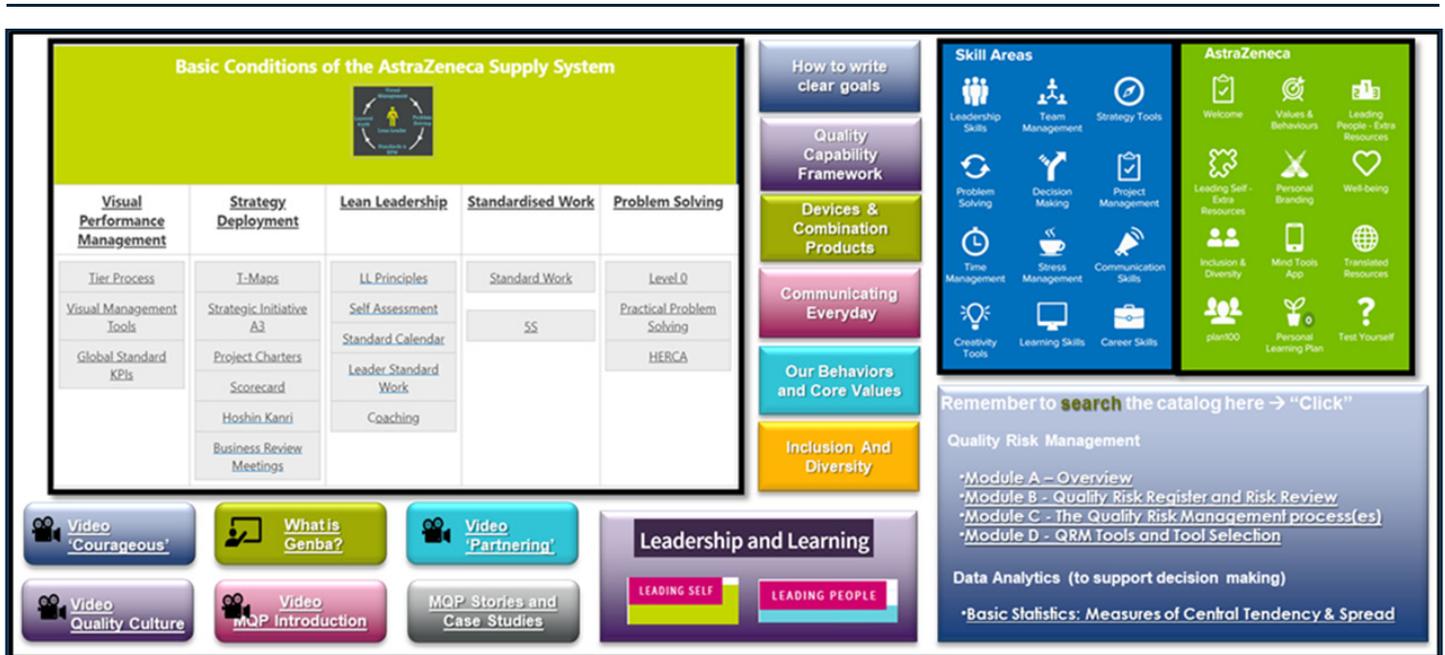


FIGURE 1 | The 10-20-70 Capability Development Model



**FIGURE 2 | Rapid Access Directory for 10% Learning towards MQP Capability Target Levels**

found in the PQL job description. The PQL works well within the CMC team. The PQL is the voice of quality in development and with the CMC teams. The PQL speaks up for quality early, takes responsibility in CMC team decisions, partners with development, and delivers to enable a streamlined development process.”

## THE MQP MODEL

The MQP development tool is intended to provide support to individuals “in their lifelong learning journey,” Krause emphasized. Underpinning it is a three-prong approach that includes a basic training curriculum, coaching and shadowing, and the repetition of core job tasks (**Figure 1**).

The basic training, he explained—on standard operating procedures and fundamentals of the GMP world—comprises about 10% of the curriculum. Another 20% comes from coaching and shadowing, attending conferences/workshops to learn what others are doing, and participating in discussions and networking.

However, the greatest contribution toward higher capability learning, Krause said, is learning by doing. “By repetition of routine job tasks, we learn how to do our job better. We can look for where we can improve things, where we can standardize things, and where we can interact better and more with our partners.”

He provided a more detailed look at the modules used in the “basic training” piece of the development tool. These modules comprise a directory including links to the resources the company makes available (**Figure 2**). Krause noted that the slide is simplified for purposes of presentation.

By repetition of routine job tasks, we learn how to do our job better. We can look for where we can improve things, where we can standardize things, and where we can interact better and more with our partners.

He explained that the training directory includes links to the various videos and documents that are part of the training curriculum.

“There are videos available on quality culture, on things that are associated with the Modern Quality Professional, and on leadership and learning. One button links to the quality capability framework. It contains a lot of the information on what it takes to reach a higher quality capability level for each quality area, such as auditing, qualification validation, quality risk management, change controls, etc.”



**FIGURE 3 | Standardized Capability Levels**

Because job tasks that need to be performed require different levels of knowledge about the various systems and subject matter, the company developed a set of definitions for a hierarchy of capability levels (**Figure 3**).

AstraZeneca evaluated the various functions that are performed by the PQL and ranked the training and knowledge required by each, resulting in capability target levels with proficiencies that map to the capability levels (**Figure 4**).

The MQP program has not only identified the capabilities necessary but provides the relevant training and experience to achieve its aims.

“We took the MQP capability areas and we picked the ones for the product quality leader that fit our job—that had relevant parts in it that we do on a routine basis, such as doing change control,” Krause explained.

“There is an area of statistics that is trending, which is needed

for some of the review tasks that we do in our role of product quality reviews. We identified those, focused on those, and then we set what we thought were the right target levels.”

For example, he said, a target level of two was set for statistics and trending, and a target level of three for change control.

“You would need an understanding of statistics to really approve product specifications because they are typically calculated,” Krause pointed out. “To do this well, you must have some basic understanding of stats and trending. These are actionable points. Now that we have actionable points, we could now essentially establish this for all our areas that are relevant for us.”

Capability target levels were set taking into account job task frequency and criticality considerations—for example, the number and criticality of specific review and approval tasks and the potential for the tasks to impact the patient or the business.

## BALANCING REQUIREMENTS AND TRAINING

Krause emphasized the importance of balancing requirements and the training conducted and experiences provided.

Capability	Target PQL Capability Level
Analytical – Chemistry	3 (Professional)
Analytical – Microbiology	3 (Professional)
Statistics & Trending	2 (Competent)
Auditing	2 (Competent)
Change Control	3 (Professional)
Documentation	3 (Professional)
Quality Risk Management	3 (Professional)
Process & Product Knowledge	3 (Professional)
Product Technical Support	2 (Competent)
Qualification & Validation	2 (Competent)
Quality & Compliance Management	2 (Competent)
Investigation & Problem Solving	2 (Competent)
Medical Devices and Combination Products	3 (Professional)
Regulatory	2 (Competent)
Data Review & Product Release	2 (Competent)
Quality Training	3 (Professional)
QA Supplier Management	1 (Foundational)

**FIGURE 4 | Relevant MQP Capability Categories and Assigned Target Levels**



**FIGURE 5 | Change Control Example**

“We can either be informed or we can be a reviewer, an adviser, or we can be the decider—it has to be one of those three,” he said. And the training and experiences provided must be commensurate with the knowledge level required and the role of the individual.

He provided a graphic illustration (**Figure 5**).

“For something as complex as change control,” Krause said, “you need to have an adequate level of understanding of statistics and trending as well as quality risk management.”

He commented that “it takes years” to complete enough repetitions of the change control activity to be competent. “We want to see no less than 15 change control records completed for product specifications.” The number of

repetitions and time to complete them varies depending on the activity.

### SOFT SKILLS ALSO IMPORTANT

In addition to technical competence, another key element of a successful leader is a set of attributes commonly called “soft skills.” Krause characterized that skill set as “important” and “difficult to measure.”

“For example,” he said, “How adaptable are we? How do we work with ambiguity? How often and how well are we speaking out? How can we influence others?”

“We are currently working on having similar ladders and similar progression towards these soft skills and higher levels of soft skills. But as you can imagine, it is more difficult to establish and implement.” ■

## HOW TO ASSESS AND ADVANCE A PHARMA COMPANY'S QUALITY MATURITY

Is your company's quality management system (QMS) proactive or reactive? Does your company use data, predictive analytics, statistics, process capabilities, and other tools to help reduce quality anomalies that in the past have led to complaints and other issues? Or does it only react and make changes to the QMS when issues and crises arise?

FDA's Quality Maturity Model (QMM) program looks at various factors in a company and how the firm administers and updates its QMS. The QMS is a collection of business processes necessary to consistently implement and maintain quality of product in the marketplace. It is not specific to drugs.

Less mature quality management systems are generally reactive. They look back. They collect general or non-specific metrics about their processes and are primarily aimed at simply achieving compliance with CGMP.

Stronger, more mature quality management systems identify sustainable compliance by focusing on performance and continual improvement and linking the metrics that measure

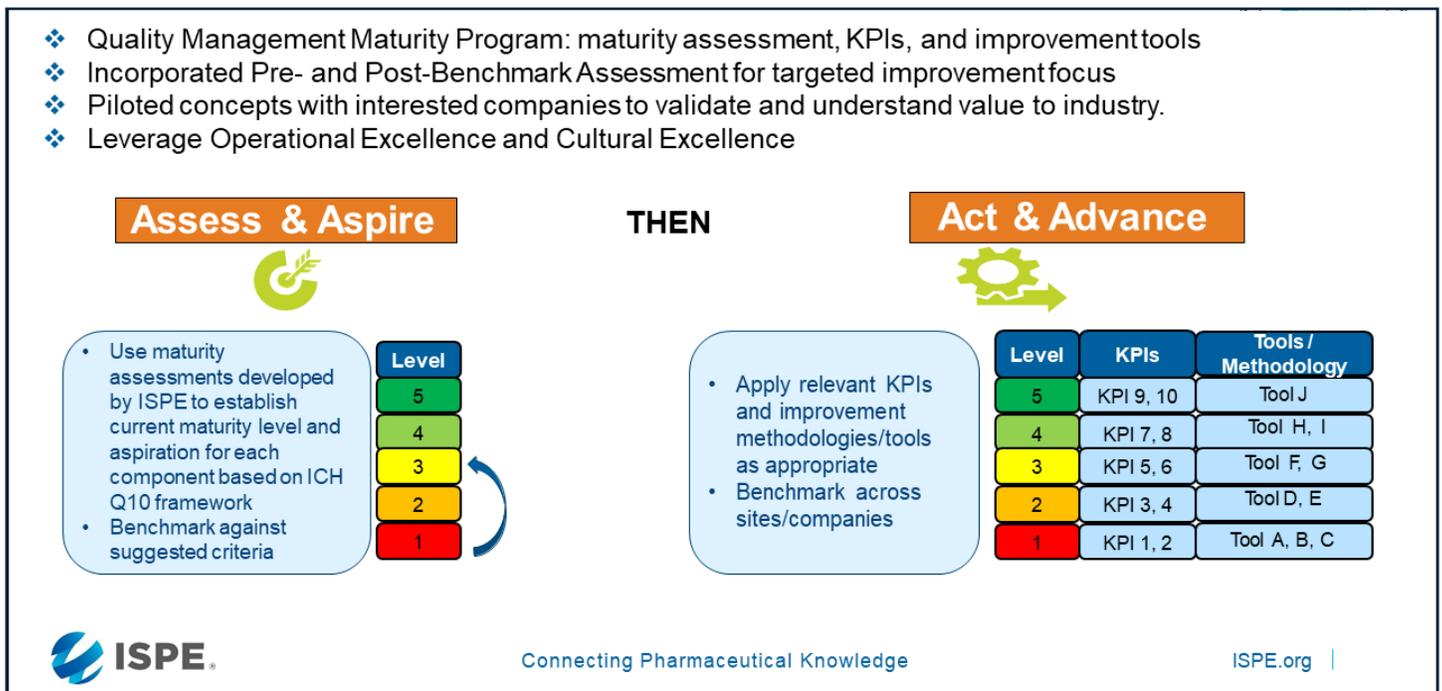
what success and improving on success looks like and that are tied to the patient. At PharmaLink 2021 co-sponsored by FDA and Xavier Health, Perrigo Corporate Quality Systems Senior Director and International Society for Pharmaceutical Engineering (ISPE) Advancing Pharmaceutical Quality (APQ) team chair Tami Frederick reviewed an effort being facilitated by ISPE aimed at helping companies achieve quality management maturity.

[Author's Note: For background and a review of the FDA QMM program as explained by FDA CDER Office of Pharmaceutical Quality (OPQ) Office of Policy for Pharmaceutical Quality (OPPQ) Director Ashley Boam, see page 13.]

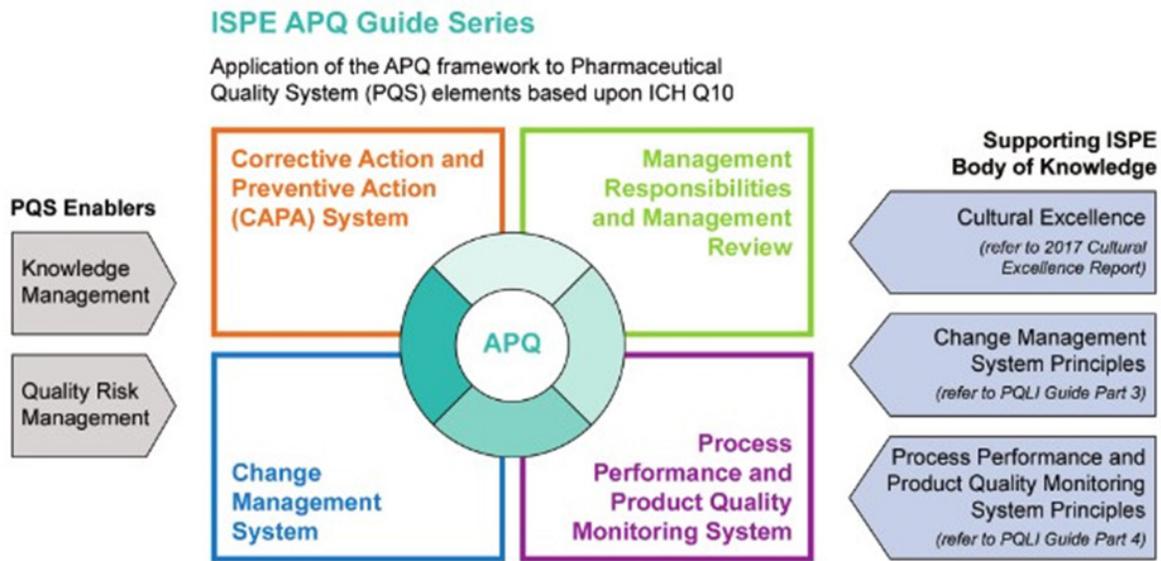
## ADVANCING PHARMACEUTICAL QUALITY

The ISPE APQ program is an industry-led effort that seeks to help companies understand the state of pharmaceutical quality within their company. It is based on the ICH Q10 framework, and ties in Product Quality System (PQS) effectiveness elements and enablers, Frederick explained.

She noted that the goals of the effort are to provide and support industry, incentivize sustained, continual improvement in each company's PQS, and allow for benchmarking.



**FIGURE 6 | APQ Framework Based upon ICH Q10**



**FIGURE 7 | ISPE Advancing Pharmaceutical Quality Program**

“This will help to increase the reliability of supply for our patients and for the consumers of our products,” she said. “It also provides better insight for health agencies like FDA and MHRA, who have been involved in these programs and have provided great feedback. They have helped us to assess the program and to make sure that it aligns with the Quality Management Maturity program overall.

The APQ framework (**Figure 6**) involves a circular pattern consisting of the following steps:

- Assess quality maturity and align it within the quality management areas
- Understand the current position
- Aspire to improve
- Make improvement actions based on metrics provided by the APQ program
- Repeat the cycle to continually improve quality maturity

Frederick explained that both St. Gallen University and Dun and Bradstreet studies helped inform the design and the processes that were used.

## ISPE PQLI COMBINES THE PIECES

ISPE’s Product Quality Lifecycle Implementation (PQLI) initiative was created to provide guidance on implementation of the concepts described in ICH guidelines, focusing on Q8, Q9, Q10,

Q11, and Q12. The effort aims to help ensure product quality throughout a product lifecycle, leading to continuous product improvement.

Frederick noted that included in this effort are “Good Practice Guides” that can be used to aid in quality maturity assessment by tying together four core areas of the assessment (**Figure 7**)

“The first one is fully published,” she said—Corrective and Preventive Actions. The second two are being finalized—Management Responsibilities and Management Review, in which two ICH elements have been combined. Also being finalized is the guide on the Change Management System.

In development are guides for the Process Performance and Product Quality Monitoring rubric for Maturity Assessment. “This will be a full Quality Management Maturity Assessment Program that the industry can take, can use themselves, can improve on themselves, and really help themselves to advance and move forward as well,” Frederick emphasized.

The program has been reviewed within industry by many experts and by FDA, MHRA, and several other health authorities, as well as by St. Gallen University and Dun and Bradstreet as well.

“We have had a lot of great feedback from many different expert teams to make sure that we are aligning a program that can work for industry—that can be developed for industry and used within industry,” she concluded. ■

## SYNERGY AT THE INTERSECTION OF DATA INTEGRITY AND QUALITY CULTURE

### ALCOA

The importance of data integrity and the idea of quality culture—what it is and how to measure and promote it—have been important topics in the dialogue within the pharmaceutical industry and with its regulators for several years. An important question that needs to be explored further is how efforts can promote both and be synergistic.

At the PDA Annual Meeting held virtually in March 2021, ValSource consultant and former Pfizer and Merck executive and PDA board member Chris Smalley provided his insight into the relationship between quality culture and data integrity in a presentation titled, “The Role of Quality Culture in Assuring Data Integrity.”

Smalley began his talk with a discussion of the elements of data integrity and followed up with a discussion of quality culture and how efforts can be aimed synergistically at both.

Smalley introduced the acronym ALCOA, which stands for attributable, legible, “contemporaneously recorded or true copy,” original, and accurate. He used the definition as the basis for his discussion of data integrity (**Figure 8**).

Smalley acknowledged that many employees are not necessarily involved in the capture or generation of data. Many are instead involved in the review or analysis of data, or may work in the storage and archival of data, disposition, or other steps in the data lifecycle.

Although the focus of his session was on the generation and creation of data, “all the other areas in the lifecycle are directly relatable to the role of quality culture,” he maintained. “And I think that will be evident as we move forward.”

### ASSESSING QUALITY CULTURE

As a beginning point for assessing quality culture, Smalley asked, “If you took a poll in your organization, would people provide honest answers to work-related questions? Or would they provide the answers that they think you are looking for?”

### ALCOA Definitions

- **Attributable:** It should be possible to identify the individual or computerized system that performed the recorded task. The need to document who performed the task / function is, in part, to demonstrate that the function was performed by trained and qualified personnel. This applies to changes made to records as well: corrections, deletions, changes, etc.
- **Legible:** All records must be legible – the information must be readable for it to be of any use. This applies to all information that would be required to be considered Complete, including all Original records or entries. Where the ‘dynamic’ nature of electronic data (the ability to search, query, trend, etc.) is important to the content and meaning of the record, the ability to interact with the data using a suitable application is important to the ‘availability’ of the record.
- **Contemporaneous:** The evidence of actions, events or decisions should be recorded as they take place. This documentation should serve as an accurate attestation of what was done, or what was decided and why, i.e., what influenced the decision at that time.
- **Original:** The original record can be described as the first capture of information, whether recorded on paper (static) or electronically (usually dynamic, depending on the complexity of the system). Information that is originally captured in a dynamic state should remain available in that state.
- **Accurate:** Ensuring results and records are accurate is achieved through many elements of a robust pharmaceutical quality system. This can be composed of:
  - equipment-related factors such as qualification, calibration, maintenance and computer validation.
  - policies and procedures to control actions and behaviors, including data review procedures to verify adherence to procedural requirements – deviation management including root cause analysis, impact assessments and CAPA
  - trained and qualified personnel who understand the importance of following established procedures and documenting their actions and decisions.

Together, these elements aim to ensure the accuracy of information, including scientific data that is used to make critical decisions about the quality of products.

**FIGURE 8 | ALCOA Definitions**

A slogan used in a lot of organizations is, “we are all team players.” If you take a poll, he suggested, even though it might be anonymous, many people would be inclined to say, “I am going to answer this in this particular way because I am a team player.”

But if you can get into their heads and really understand how employees perceive the culture, what would they be thinking?

Would a person that works in your organization say, “If I get caught making a mistake, I will be disciplined or fired.”?

Would an employee say, “That is not really my job. I am going to do my job. And that other activity, that is someone else’s responsibility. And I am not going to get involved in that. I am not going to comment on that. I am not going to help with that because it is not my job.”?

Do employees have a perception that they are not important? That they are just at work doing the daily grind day in and day out—just a cog in the wheel who nobody pays attention to?

Or maybe you would find employees who believe that they are valued. And one of the reasons they believe they are valued is because the organization gives them the tools and resources they need to be successful at their job.

How do we avoid employees thinking those first three ways or many other variations to those first three, and work our way towards employees who feel that they are valued—that they are appreciated and get what they need to be able to do their job right?

## TRAINING AND EDUCATION ARE KEY

“I am a tremendous fan of training and education,” Smalley emphasized. “I think training and education are necessary to achieve a quality culture. That is one aspect. Saying that I am a big fan does not mean it is the only activity that you should engage in. But it is a key activity—an important aspect of changing your quality culture, if you believe your quality culture is not where you want it to be. And if you do have a good quality culture, it is important in maintaining it.”

Training in a quality culture is not just having people sit at a computer online and read an SOP, and at the end of the SOP click that they have read and understood it, he stressed.

“It is not just a matter of having them assemble in a room and be warm bodies in chairs while someone talks ‘at them.’ I am

deliberate in my use of the term ‘at them,’—not talking to them, but talking at them.”

People do not feel valued when being talked at or lectured, Smalley maintained. People do not feel like you are connecting with them. It makes them feel minimized. It makes them feel that you are valuing convenience over what they are contributing to your organization.

## Smalley acknowledged that many employees are not necessarily involved in the capture or generation of data

“If you look at your entire organization and you look at your facilities and your equipment, your employees are really a valuable asset,” Smalley stressed. “You take care of your facilities. You take care of your equipment. You need to do the type of job where you take care of your employees where your employees feel that, in fact, they are being taken care of.”

## THE RIGHT TRAINING IN THE RIGHT WAY SUPPORTS QUALITY CULTURE

How do you conduct training and education if you want to achieve a quality culture? Instead of employees being online by themselves reading an SOP where maybe they read the words but really do not understand it and click that they read and understood it, or sitting in a room—there is an interactive activity.

Training means conducting interactive workshops. It means providing training and then stopping and allowing people to work in small groups or maybe with people from other departments to talk about what they have experienced or learned.

It is good if the employee comes back and presents to the rest of the group so the trainers understand what their interpretation was, what happened, and how they processed the information that was presented to them and understood it.

It is important with this sort of training that facilitators are used who are not the employees’ supervisors and managers. Because when people are being trained by their supervisor and manager, it can discourage questions.

People do not want to say to their supervisor or manager, “I do

not understand. I do not understand that procedure,” because they are afraid that the supervisor or manager will say, “Well, this is just a revision of an existing procedure. You should have been following this all along. Are you stupid?”

## Training in a quality culture is not just having people sit at a computer online and read an SOP

They do not want to take the chance. Maybe their supervisor or manager is more empathetic than that, but they do not want to take the chance that the supervisor or manager is going to think that they are not smart, that they do not understand. They are not going to ask that question. So, use a facilitator. The employees need to see that management is committed to the training.

All too often, training is thought of as just a budget item, and opportunities for important training are missed because there is not enough money in the budget.

Obviously, there cannot be an unlimited pool of money for training. But it should not just constantly be a situation where the department only has limited resources to support the employees and train them.

Management should be in a position to say, “That might not be the right training for you, so we are not going to send you to that conference. Or we are not going to send you to that course. But when the right training and the right course comes along for your job and your role, and it helps develop you, you are certainly going to be sent to that course. You are certainly going to have an opportunity to take that training, because we value you as an employee.”

## HOW DOES WHAT I DO MAKE A DIFFERENCE?

Another aspect of training and education under the umbrella of a quality culture is employees’ understanding of the importance of their particular job, how that activity relates to the final product, and how it contributes to a product that the patient finally receives.

If a patient is going to receive a vaccine—for example, a

COVID-19 vaccine—it is not because of the training at their company and their quality culture that the employee understands their importance. They understand it simply by going home and looking at the news and talking to their families.

Because in the news and in their family, they are hearing, “I am doing an important job. I am contributing to something that is really important in this worldwide pandemic.” And they are proud to say, “I work for this company. I am a contributor.”

It does not matter whether they are responsible for cleaning the aseptic processing rooms or washing equipment or are involved in the process or compounding or filling or inspecting or labeling or packaging or working in the warehouse—every job is important. And every person should know that his or her job is contributing to the product getting to the patient.

“They need to hear that. They need to hear that in their training, in their education, from their management, that their job is an important part of supplying the patient with the product.”

## HOW MY JOB MATTERS

The importance of someone cleaning the aseptic filling room is assuring that that vaccine is not going to be contaminated, either microbiologically or cross-contaminated with another product, should be explained.

The person in the warehouse needs to understand the importance of assuring that materials that are rejected, materials that are quarantined are kept separate and are controlled, and only approved material is shipped and gets to the patient.

## The employees need to see that management is committed to the training

The person who is responsible for clean equipment is going to understand the issues of cross-contamination and the issues of equipment operating properly, because they clean it and reassemble it.

And the employee actions are going to be documented. That documentation is going to be part of the data integrity system. In every step of the process, people should be proud of their job, and they should welcome the opportunity to record that they did their job, Smalley maintained.

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## TAKING PRIDE IN THE JOB

At a company with a strong quality culture, employees are proud to be part of the company and take pride in their contributions.

For example, a cleaning technician might think or say, “I cleaned this room, and I signed that I cleaned this room. Or this is how I compounded the cleaning solution, how much cleaning concentrate I used, how much water for injection I used to compound the solution. Or this is how I cleaned this piece of equipment. I followed the process. I followed the SOPs and inspected the equipment. And I labeled the piece of equipment as clean and moved it to the right location.”

**In every step of the process, people should be proud of their job, and they should welcome the opportunity to record that they did their job**

Everyone is contributing to the final product. And when they contribute to the final product, they then have a tremendous difference in their attitude towards data integrity—towards the importance of their job and what they sign.

## KNOW THE CUSTOMER

Everyone should understand the importance of their role. Everyone in the process should know who their customer is—specifically, their internal customer.

“I am not talking about the patient or the clinician,” the Valsource consultant pointed out. “I am talking about their internal customer.”

“The person who cleans the aseptic filling room knows his or her customer is the team that is going to go in and use that room and perform the aseptic process in that room. The person cleaning a piece of equipment should know that the customer is going to be the team that goes in and uses that piece of equipment for compounding.”

Everyone should know who their customer is and what their customer needs are. “And you always want to satisfy the needs of your customer. So, you must get to know your customer. You are not invisible to your customer. Getting to know your customer

is part of the quality culture as is your role contributing to the product that that patient or that clinician will eventually see,” Smalley said.

## SUPPORTING THE EMPLOYEES

In addition to education and training, it is important to ensure that employees have the resources they need. Education and training are resources. But people need other resources as well.

For example, they need to have equipment available. The equipment needs to be qualified or validated. It needs to be calibrated where appropriate.

They need to have adequate time to do their job, and they need a buddy checking with them.

“I am not talking about checking or verifying that I weighed out the right amount of material before I take it off the balance,” Smalley clarified. That is the second-person verifier, not the buddy.

Sometimes people perform jobs by themselves—for example, a person is in an aseptic filling room alone mopping the room. Or a person in a washroom by himself or herself washing a tank or washing a piece of equipment. They should have people that are coming around and checking on them—a buddy, so to speak.

It is important from a safety standpoint, but it is not just from a safety standpoint. It is to say, “You are a valued employee. You are important to us, and we are not going to let you work eight hours or four hours or even two hours without someone checking on you to see how you are doing because we care about you.” You must make them feel like a valued employee.

## CASE STUDY: NO GOOD CHOICE

Smalley presented a hypothetical case study involving a laboratory chemist who received samples from two batches towards the end of the day on a Friday—a situation that seems to happen all too frequently.

The chemist had made a promise to her son that she would take him to his soccer game. He is going to be playing in the game. She made a promise that she is going to take him to the game and stay and watch.

By the time the tests are completed on the first of the two

batches, it is going to be very close to the time that she would ordinarily leave at the end of the workday, which would be the time she planned to leave to go home to take her son to the soccer game.

The organization has made it clear that it does not permit samples to be tested later. She does not have a choice to take that sample, put it in the freezer, and take it out of the freezer on Monday and test it. The chemist rationalizes. This is a rationalization process that can affect data integrity.

She rationalizes, “Both these batches were made by the same production team, on the same equipment on the same day, on Friday—they should be the same. So, I can reuse the test. I can go into the system and I can change the header so the batch number and the time the test was run will look different. I can have two results—one from batch one and one for batch two, but it will only take me the time it took to run one batch. And that way I can leave and go to the game.”

People who are in control of the quality culture are the people who are responsible for scheduling the workload. This laboratory analyst did not have the resources she needed to do the job. Organizations are particularly good about scheduling production, but they do not seem to be as good about scheduling the laboratory sample receipt testing.

## ENABLE BETTER CHOICES

If the samples come into the lab late in the day, perhaps a second shift should be arranged, or maybe there should be some sort of split shifts or overlapping shifts for better coverage.

Another batch was added on Friday. When they added that batch, they should have planned for overtime so that the analyst who was going to work Friday would have known that she would have to stay late. And maybe she could have asked for volunteers to work late.

People make choices in their work/life balance. Putting that lab analyst in the predicament described is putting her into a trap. She made a promise to her child. That is important in her life. It is important as a parent.

Part of her job is testing samples. “You are creating a conundrum where she must make a choice. And either choice is going to be a poor choice for her. That is not a quality culture. You do not create that situation. You prevent creating that situation. You tell people that they are a valued resource by planning better,” Smalley stressed.

The production scheduling should work better. The way in which the laboratory is scheduled should be perhaps planned better, or allowances should be made, if possible, for freezing the sample and allowing it to be tested on Monday.

## SLOW DOWN AND FOCUS

In your company, if you want to assure data integrity, do you have the time to do your job properly? Smalley asked. Or do you feel you are rushed to do your job?

Do you have a quiet space you can use to concentrate when you need to perform some tasks so that you are not subject to distractions?

There are some companies that run yellow tape across the front of the office or cubicle of an individual who is doing a crucial review such as a batch record review or maybe a review for a CMC section for an NDA. The caution tape tells everyone not to disturb the person—that he or she is involved in something that needs focus and concentration and cannot be distracted.

“These examples that I have given you illustrate the intersection between quality culture and data integrity. Give people training and resources. Give employees the tools to prevent them from having to make bad choices,” Smalley advised. ■

## ASHLEY BOAM ON FDA'S PROPOSED QUALITY MATURITY MODEL

FDA is proposing the use of a model that would measure and rate the maturity of a pharma company facility's quality management system. This model would eventually incentivize companies to improve their ratings in exchange for regulatory concessions such as flexibility in post-approval change management. FDA would not disclose a company's rating, although companies could potentially share their ratings to differentiate their products based on quality for consumers and other purchasers.

At the 2020 PDA Annual Meeting held virtually in July, FDA CDER Office of Pharmaceutical Quality (OPQ), Office of Policy for Pharmaceutical Quality (OPPQ) Director [Ashley Boam](#) discussed the proposed Quality Maturity Model (QMM). She positioned it as the next step in a progression that began in 2004 with the [Pharmaceutical Quality for the 21st century report](#) that laid out a vision of a "maximally efficient, agile, flexible manufacturing sector that reliably produces high quality drug products without extensive regulatory oversight."

She explained that CGMP is a minimum standard for systems that assure proper design and monitoring and controls for manufacturing processes and their facilities. But to fully realize the pharmaceutical quality vision for the 21st century "requires moving more of the manufacturing sector into richer quality management systems."

Boam notes that additional context for this topic came up in a [report that FDA issued in October of 2019 on drug shortages](#), in which the agency looked at a number of factors and what might be causing drug shortages, as well as potential solutions to those issues.

The report identified three root causes for drug shortages, including that the market does not currently recognize and reward manufacturers who have mature quality management systems that focus on continuous improvement and early detection of supply chain issues that can lead to a drug shortage. One of the solutions recommended in the report was to develop a rating system to incentivize drug manufacturers to invest in quality management maturity and to incentivize purchasers to recognize and reward QMM.

## FROM GMPS TO ICH Q10 TO QMM

CGMP is defined in the regulations for drugs in 21 CFR 211 for drug products and in ICH Q7: *Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients*. It sets out minimum expectations for quality. Regarding improvement, 21 CFR 211 outlines what is referred to as the at least annual product review, where a manufacturer is expected to go back and review a representative number of batches as well as complaints and recalls other quality defect reports to identify where there may have been issues in the process or product that should be addressed.

Similarly, ICH Q7 calls for a product quality review of APIs, looking for opportunities to verify and improve the consistency of the process.

ICH Q10: *Pharmaceutical Quality System* moved industry a step forward because it augments the concept of CGMP with the idea of the effective pharmaceutical quality system, which covers the entire lifecycle of the product.

Q10 walks through several sets of activities that should be conducted to not only manage but continually improve the pharmaceutical quality system. It also describes how knowledge management and quality risk management principles enable continual improvement. ICH Q10 looks back as well as forward and promotes taking steps to improve (**Figure 9**).

"How do we get to this idea of quality management maturity?" Boam asked. "The quality management system is a collection of

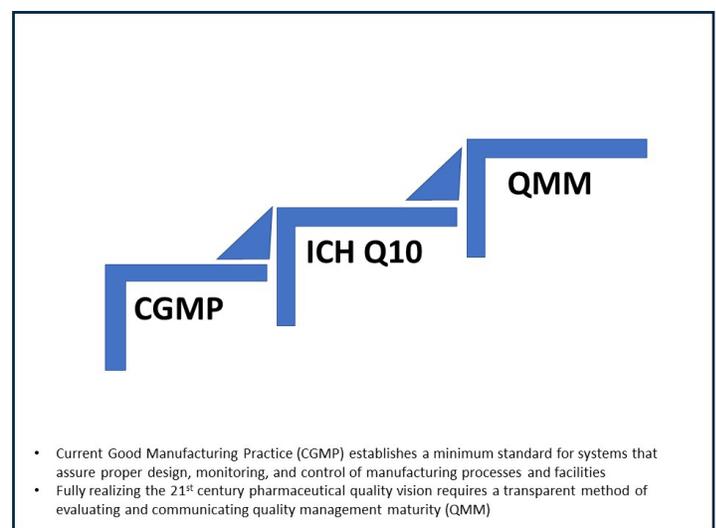


FIGURE 9 | Steps to QMM

business processes that are needed to consistently implement and maintain quality of product in the marketplace. It is not specific to drugs. It is not a new concept.”

“What we see in the pharmaceutical sector is that less mature quality management systems are generally reactive. They look back. They collect general or non-specific metrics about their processes and are primarily aimed at simply achieving compliance with CGMP.”

Stronger, more mature quality management systems look for sustainable compliance by focusing on performance and continual improvement and linking the metrics that talk about what success and improving on success looks like and that are tied to the patient.

These types of systems use data, predictive analytics, statistics, process capabilities, and other tools to help reduce quality issues that in the past have led to complaints, looking, for example, at supply disruptions and shortages.

“The quality management maturity umbrella, if you want to think about it that way, has lots of different components to it,” Boam pointed out. **(Figure 10)**

“You see here under this umbrella we have performance management and continual improvement, quality culture, predictive analytics, and supply chain management, to mention a few. A big piece that comes from ICH Q10 is management review and responsibility. One way to think of quality management maturity is how well and how thoroughly are you implementing ICH Q10?”



**FIGURE 10 | Quality Management Maturity Umbrella**

Quality systems shape culture. Quality culture is a big piece of quality management maturity. This is where the people come into play. A culture of quality is what is necessary to achieve these higher levels of maturity.

Focusing on innovation and continual improvement means identifying opportunities and then acting on those opportunities to improve the product quality system and to improve other aspects of the manufacturing process.

Moving into performance-based quality management means using data to drive actions and improvements. Part of that may be a robust metrics program with a focus on analytics and using those metrics to help identify areas for improvement.

## WHAT DOES QMM LOOK LIKE?

What does quality management maturity look like? **(Figure 11)**.

QMM is embodied by manufacturers and as well as those who have responsibility for oversight and controls over manufacturing taking ownership for quality. That starts from the top. Management sets the tone for a commitment to quality. “We see investment in people, because it cannot just be those at the top—it must be folks at every level of the organization contributing to that commitment to quality to result in quality product,” Boam emphasized.

QMM is demonstrated by organizations where the objectives are set to drive equality. They are not business objectives and quality objectives, but they are linked together.

**Manufacturers and those with oversight and controls over manufacturing take ownership for quality:**

- Management sets the tone of commitment to quality
- Invest in people
- Organizational objectives drive quality
- Quality systems shape culture
- Focus on innovation and continual improvement
- Move to performance-based quality management
- Robust metrics program with a focus on analytics
- Include risk management plans and forecasting to ensure reliability of supply



**FIGURE 11 | What QMM Looks Like**

Another element FDA sees as part of quality management maturity is the use of risk management plans and forecasting to be prepared for potential interruptions in the supply chain to ensure that there are contingencies in place and that these types of interruptions will not lead to an interruption in supply.

[Related: Busy quality leaders can stay on top of FDA 483 observation trends by downloading a personalized 483 observation report for free here.]

## THE BENEFITS OF QMM

The benefits of QMM, Boam maintained, apply to patients and consumers as well as to industry and FDA.

In terms of patients and consumers, important medications are too often in shortage and not available for patients who need them. This means that quality management systems have to be more robust to help eliminate and minimize the potential for supply disruptions. This results in providing more reliable access to patients and consumers as well as fewer quality related issues that could lead to a supply disruption or a recall.

In terms of industry, we see this as fitting well within the requirement in section 501 of the statute that requires manufacturers to have oversight and control over the manufacturer of their drugs.

“In addition, we see more advanced levels of quality management maturity leading to fewer recalls, a better corporate image, and enabling improvement of not only process performance and

## Management sets the tone for a commitment to quality.

product quality but also the pharmaceutical quality system as we saw in ICH Q10,” Boam said. “Overall, it leads to quality system efficiencies, cost savings and regulatory flexibility.”

There are benefits to FDA as well. QMM will provide additional quantitative and objective insight into the state of quality for products and facilities, which means that the agency will have better information as it considers where the risks exist in facilities that it needs to prioritize for surveillance inspections on a yearly basis.

“When we do go out and inspect, understanding the quality management maturity in that facility gives us an opportunity

to be more focused in the inspection, which then may lead to a shorter overall inspection because we have a better idea of where we need to focus,” she maintained.

Importantly, quality management maturity also facilitates a more flexible regulatory approach, including implementation of ICH Q12 tools such as established conditions. “This is where we start to get more toward the goal of high-quality drug products being regulated without extensive regulatory oversight.”

From a CDER perspective, FDA has identified the need, as evidenced by the drug shortage report, for a system to measure and rate a drug manufacturing facility’s quality management maturity and its ability to deliver high-quality drug products reliably and without disruption.

## INCENTIVIZING MANUFACTURERS

The agency wants to be able to incentivize manufacturers to improve their quality management systems by rewarding those that achieve a high degree of maturity by encouraging the facility to provide transparency about its high level of maturity to purchasers, so that purchasers might choose to reward facilities that have a higher level of maturity when choosing where to make their purchasing decisions.

“Overall, we see implementing and improving and incentivizing levels of higher management maturity as reducing the likelihood of quality problems that could lead to drug shortages, because it will improve the robustness of quality management systems in general,” Boam explained.

Regarding the umbrella of quality management maturity (**Figure 10**), “I want to call your attention to the piece here on quality metrics. How do quality metrics fit into the idea of quality management maturity? We see quality metrics as a piece under that umbrella, and a key aspect of a mature quality management system.”

One of the characteristics of a mature quality management system is using data-driven approaches to reduce quality issues. And when you think about how FDA might be able to evaluate and establish a rating for a facility’s quality management maturity, that would likely be done through an assessment, which would represent an evaluation at a point in time.

“Quality metrics data would be important to provide information about what is going on in that facility in between on-site assessments,

providing ongoing confidence that what we saw in an assessment of the firm's quality management maturity is continuing to play out as time goes by," the OPPQ Director maintained.

## BUILDING A QMM SYSTEM

Regarding building a quality management maturity program, Boam explained that first it makes sense to learn from the efforts that have been completed and are still ongoing at this point:

- The PDA Quality Culture Initiative
- The ISPE Advancing Pharmaceutical Quality program
- Research and ongoing work from the University of St. Gallen
- The CDRH Case for Quality pilot program

Second, FDA envisions this to be a voluntary program. And third, FDA plans to incorporate stakeholder input.

"There are lots of folks out there who have done a lot of work, some as part of the programs we named here, but a lot of work

**Mature quality management systems enable sustainable compliance, focus on continuous improvement, and improve supply chain robustness.**

regarding quality culture and quality management maturity, which would be a critical piece of any program," she said.

In conclusion, mature quality management systems enable sustainable compliance, focus on continuous improvement, and improve supply chain robustness. Together these result in improved business practices and increased opportunities to benefit from ICH Q12: *Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management* tools such

as established conditions, and ultimately, and most importantly, increased confidence for patients in the safety and effectiveness of their next dose.

## Q&A FOCUSES ON SHARING ASSESSMENTS

The Q&A session after Boam's presentation focused on sharing QMM assessment information with other stakeholders.

In response to a question regarding sharing of information, Boam replied, "The idea is to provide metrics to the site so that information can be shared—for example, with purchasers, who we understand are increasingly requesting supply chain information.

"They are trying to [determine the quality profile of the site] by looking at 483s and inspection outcomes that FDA makes available to make decisions about which drugs to purchase based on that information. And while inspection information is important and is something that weighs into our risk model, it is not the only piece of information.

"We believe that quality management maturity is a more holistic way to understand what is going on in the facility from a quality perspective and would be more meaningful to those making decisions about which drugs to purchase from where based on supply chain information."

Amgen Senior Advisor Steve Mendivil commented, "That could be a paradigm shift. If payers would pay a premium for higher quality and a more secure drug supply in the future, that becomes a marketing tool, enabling a company to compete in the marketplace based on quality. And that will drive quality to an even higher maturity. This could be a game-changer in the pharma industry."

"That is what we are hoping for," Boam replied. ■