# Advancing Pharmaceutical Quality:
## Quality Management Maturity Program

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# State of Quality in the Pharmaceutical Industry

FDA 21st century vision for manufacturing and quality with input from academia and industry. The desired state was described as follows:

"*A maximally efficient, agile, flexible pharmaceutical manufacturing sector that reliably produces high-quality drug products without extensive regulatory oversight.*"

"While much progress has been made, we have not fully realized our 21st century vision for manufacturing and quality."

Food and Drug Administration [Docket No. FDA-2018-N-1903] Modernizing Pharmaceutical Quality Systems; Studying Quality Metrics and Quality Culture; Quality Metrics Feedback Program, June 2018

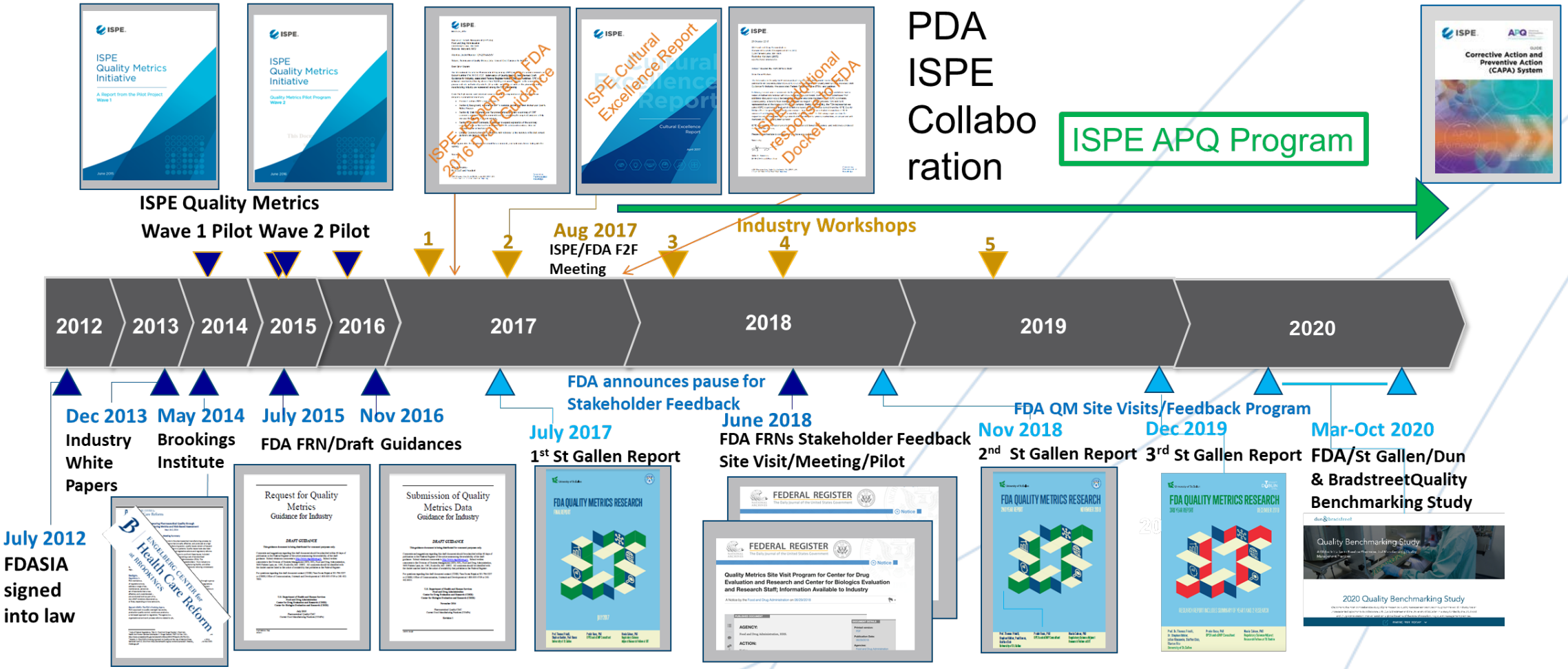
# ISPE Advancing Pharmaceutical Quality (APQ) Program Overview

- An industry-led program for advancing the state of Pharmaceutical Quality that companies could leverage to achieve the goal of ensuring a continuous supply of quality medicines to patients
- Built on the ICH Q10 framework enhanced to include operational excellence and quality culture
- Deliverables are Guides to include maturity assessments, KPIs, and continual improvement tools focused on the ICH Q10 elements
- Complementary, where possible, to current regulatory initiatives promoting quality excellence e.g. PIC/S Data Integrity Guidance, FDA New Inspection Project (NIPP), and the MHRA Data Integrity Guideline.

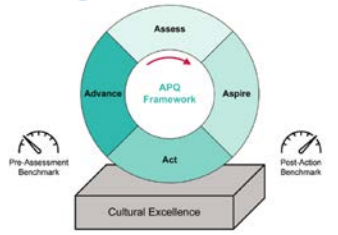
# Primary Goals of APQ Program

- Industry
  - **Supports and incentivizes sustained, continual improvement** of a firm's PQS
  - **Benchmarking & best practice sharing** to accelerate progress
- Patients and Consumers
  - **Increased reliability of supply** of quality product
- Health Agencies
  - Better insight into **industry's focus and current expectations** regarding critical quality areas for advancing pharma quality

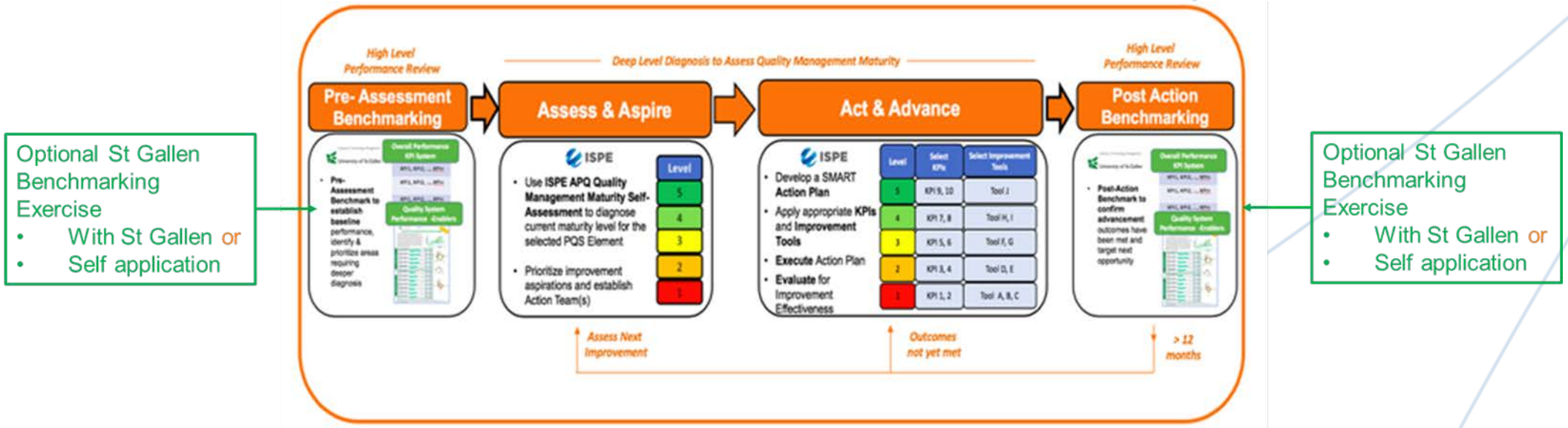
# The ISPE Quality Metrics/Advancing Pharmaceutical Quality (APQ) Timeline



# APQ Program Framework Based upon ICH Q10

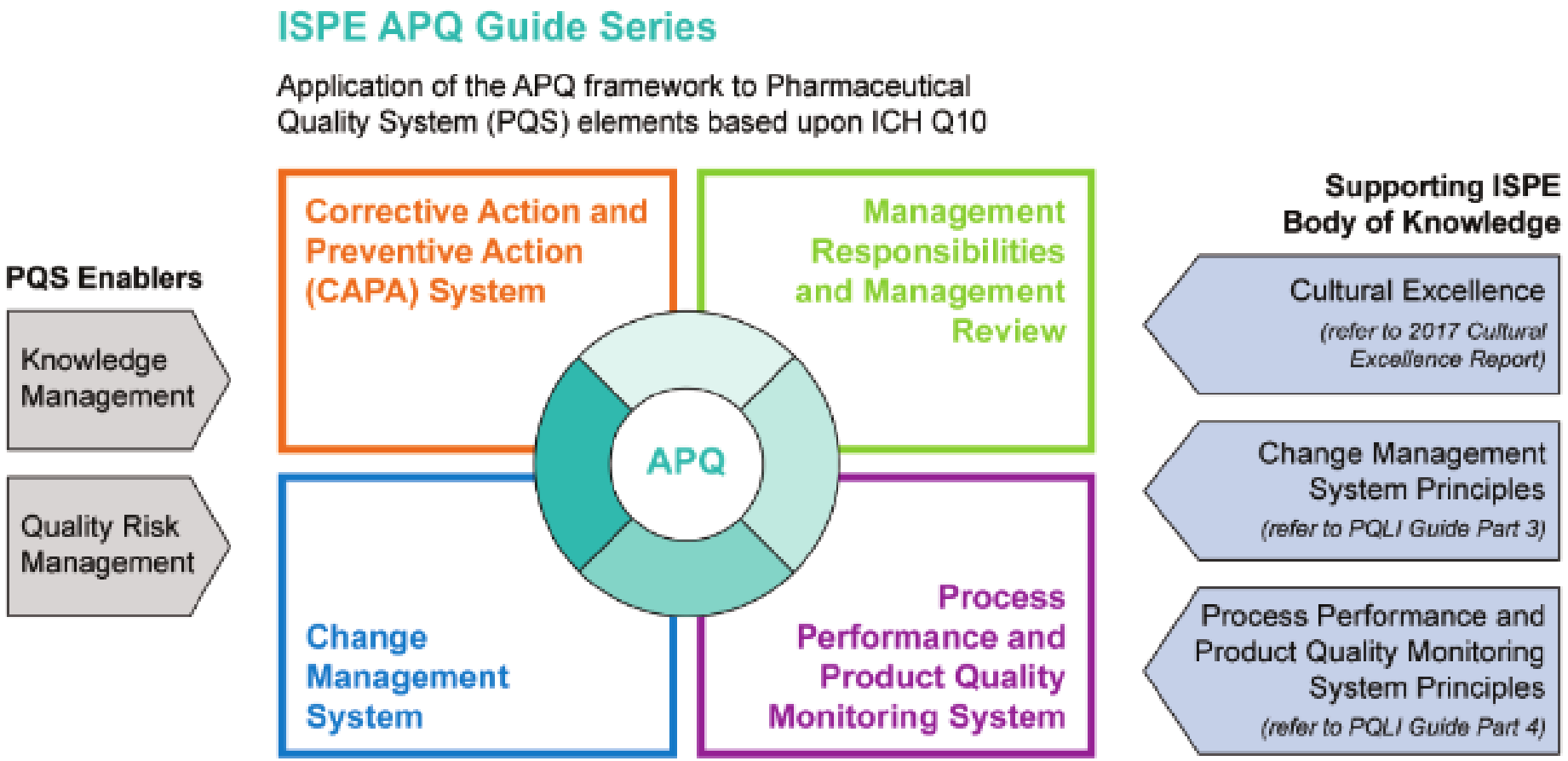



- Quality Management Maturity Program: maturity assessment, KPIs, and improvement tools
  - Assess, Aspire, Act, Advance
- Incorporated Pre- and Post-Benchmark Assessment for targeted improvement focus
- Piloted concepts with interested companies to validate and understand value to industry.
- Leverage Operational Excellence and Cultural Excellence as Foundation




The APQ Assess, Aspire, Act and Advance Framework

# ISPE Advancing Pharmaceutical Quality Program



# ISPE APQ Guide Series - Content

Each of the 4 Modules of the Guide Series will contain:

- Background of the APQ Framework
- Overview and Structure of the APQ Framework
- How to conduct the Quantitative Pre- and Post-Assessments
  - In the St Gallen Benchmarking program
    **OR**
  - By conducting internally
- How to conduct and score a deep dive **Assess and Aspire** exercise for each Q10 element
- How to set up an **Act and Advance** improvement program
- A worked example to assist practitioners

# CAPA Maturity Assessment

**Assess:** Determine overall CAPA maturity level utilizing **CAPA Maturity Assessment**.

| | Undefined | Defined | Managed | Improved | Optimized |
|---|---|---|---|---|---|
| **CAPA Maturity Area** | **Level 1** | **Level 2** | **Level 3** | **Level 4** | **Level 5** |
| | *Undefined<br>*Uncontrolled<br>*Not monitored<br>*No evidence | *Partially defined<br>*Not formally controlled<br>*Not formally monitored<br>*Person dependent | *Defined policy and processes<br>*Meets Requirements for Application<br>*Process monitoring and controls in place | *Defined policy and processes<br>*Routine application<br>*Routine monitoring, advancing improvements | *Proactive<br>*Continuous Improvement<br>*Predictive |

Maturity Assessed for each of the following areas/sub-elements of the CAPA system:

1. Documentation
2. Problem Identification
3. Root Cause Investigation
4. Corrective and/or Preventive Actions
5. Effectiveness
6. Metrics
7. Governance, Management Oversight, & CAPA Prioritization

**Level 4**

**Demonstrates improved/optimized execution**

*Defined policy and processes
*Routine application
*Routine monitoring, advancing improvements

**Aspire:** Determine what overall CAPA maturity level your company would like to achieve.

# CAPA Maturity Assessment

Overall high level descriptors for all areas →

Detailed descriptors for individual area →

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| CAPA Effectiveness | • There is no SOP and/or training that outlines that effectiveness check criteria must be established.<br>• Effectiveness checks are not completed to demonstrate that the Corrective Actions or Preventive Actions were effective at eliminating or mitigating the root cause(s) of the deviation/nonconformance or potential nonconformance (preventive action). | • A SOP and/or training exists that outlines that effectiveness check criteria must be established, however effectiveness check criteria is not always documented within the records.<br>• Effectiveness checks are sometimes completed to demonstrate that the Corrective Actions or Preventive Actions were effective at eliminating or mitigating the root cause(s) of the deviation/nonconformance or potential nonconformance (preventive action). | • A SOP and/or training exists that outlines that effectiveness check criteria must be established. The effectiveness check criteria is always documented within the records, however the criteria may not always be adequate.<br>• Effectiveness checks are always completed/documented to demonstrate that the Corrective Actions or Preventive Actions were effective at eliminating or mitigating the root cause(s) of the deviation/nonconformance or potential nonconformance (preventive action). | • A SOP and/or training exists that outlines that effectiveness check criteria must be established. The effectiveness check criteria is always documented within the records. The criteria includes the following (or equivalent):<br>o The data sources to be evaluated<br>o Quantifiable criteria to meet in order to eliminate/mitigate the deviation/nonconformance<br>o Length of time or number of opportunities to review.<br>o Statistical methodology is sometimes used<br>• Effectiveness checks are always completed/documented to demonstrate that the Corrective Actions or Preventive Actions were effective at eliminating or mitigating the root cause(s) of the deviation/nonconformance or potential nonconformance (preventive action) | • Effectiveness check process has become predictive, not only in addressing corrective actions but truly emphasizing preventive and predictive measures for effectiveness.<br>• Predictive Analytics are used to continually improve and foster a culture of preventive action within the QMS. This is engrained in the QMS processes, provides seemless network collaboration, and proactive actions to drive continual improvement.<br>• Best practices related to training are shared across the sites and network to improve overall performance. |

# CAPA Program Tool Catalogue

**CAPA Tool Catalogue**

Use: For a given maturity level, utilize recommended tools at current level as well as lower levels as appropriate.
Note: Utilizing tools at a level or two higher than current level may be considered when building an organization's capability.

| | Undefined | Defined | Managed | Improved | Optimized |
|---|---|---|---|---|---|
| **CAPA Maturity Area** | **Level 1** | **Level 2** | **Level 3** | **Level 4** | **Level 5** |
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| CAPA Documentation | | | | | |
| Problem Identification | | | | | |
| Root Cause Investigation | | | | | |
| Corrective and/or Preventive Actions | | | | | |
| CAPA Effectiveness | | | | | |
| CAPA Metrics | Recommended metrics included | | Note: Clearly define which issues or signals contribute to each metric.<br>Note: Either establish targets (based on what makes sense for your business) or use metrics to identify trends. | | |
| Governance, Management Oversight, & CAPA Prioritization | | | | | |

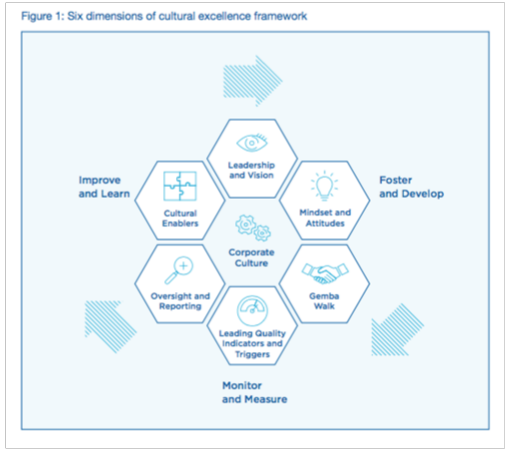
Recommended tools, KPIs, actions and procedures given

# ISPE Cultural Excellence Support Materials

- **2017 Cultural Excellence Report**

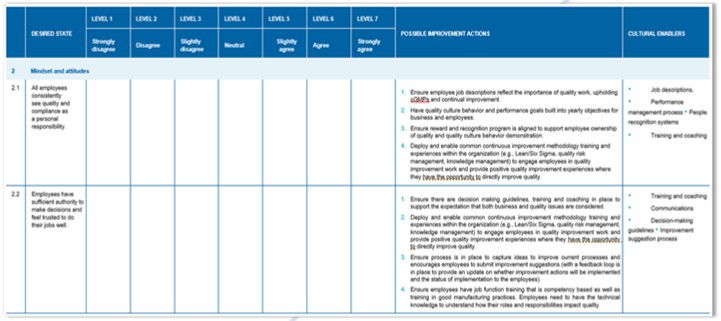
### The Six Dimensions of Cultural Excellence

A holistic framework of those elements required to foster, develop, monitor, measure, learn, and ultimately improve your organization's quality culture




Source: ISPE Cultural Excellence Report, April 2017

### Cultural Excellence Assessment Tool – Appendix 1



| | DESIRED STATE | LEVEL 1 Strongly disagree | LEVEL 2 Disagree | LEVEL 3 Slightly disagree | LEVEL 4 Neutral | LEVEL 5 Slightly agree | LEVEL 6 Agree | LEVEL 7 Strongly agree | POSSIBLE IMPROVEMENT ACTIONS | CULTURAL ENABLERS |
|---|---|---|---|---|---|---|---|---|---|---|
| 2 | Mindset and attitudes | | | | | | | | | |
| 2.1 | All employees consistently see quality and compliance as a personal responsibility. | | | | | | | | 1. Ensure employee job descriptions reflect the importance of quality work, upholding cGMPs and continual improvement.<br>2. Have quality culture behavior and performance goals built into yearly objectives for business and employees.<br>3. Ensure reward and recognition program is aligned to support employee ownership of quality and quality culture behavior demonstration.<br>4. Deploy and enable common continuous improvement methodology training and experiences within the organization (e.g., Lean/Six Sigma, quality risk management, knowledge management) to engage employees in quality improvement work and provide positive quality improvement experiences where they have the opportunity to directly improve quality. | • Job descriptions.<br>• Performance management process • People recognition systems<br>• Training and coaching |
| 2.2 | Employees have sufficient authority to make decisions and feel trusted to do their jobs well. | | | | | | | | 1. Ensure there are decision making guidelines, training and coaching in place to support the expectation that both business and quality issues are considered.<br>2. Deploy and enable common continuous improvement methodology training and experiences within the organization (e.g., Lean/Six Sigma, quality risk management, knowledge management) to engage employees in quality improvement work and provide positive quality improvement experiences where they have the opportunity to directly improve quality.<br>3. Ensure process is in place to capture ideas to improve current processes and encourages employees to submit improvement suggestions (with a feedback loop is in place to provide an update on whether improvement actions will be implemented and the status of implementation to the employees).<br>4. Ensure employees have job function training that is competency based as well as training in good manufacturing practices. Employees need to have the technical knowledge to understand how their roles and responsibilities impact quality. | • Training and coaching<br>• Communications<br>• Decision-making guidelines • Improvement suggestion process |

- **ISPE/PDA Collaboration**

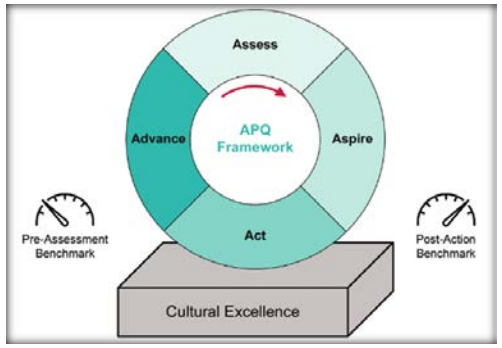
  www.ispe.org/improveculture or www.pda.org/improveculture

### Root Cause Analysis Guide

- **ISPE Cultural Excellence Report 2**

### Reward and Recognition
### GEMBA Walk

# APQ Guide Reviews




- Industry Review & Pilot
- Academia Review
- Health Authority Review

# ISPE Advancing Pharmaceutical Quality Core Team Members

| | | | |
|---|---|---|---|
| Tami Frederick | APQ Chair, Perrigo | Harry Jeffreys | Bausch Health |
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| Andrew Denny | Bristol Meyers Squibb | Chris Potter | ISPE |
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| Kira Ford | Eli Lilly | Nelson Webb | Proctor and Gamble |
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