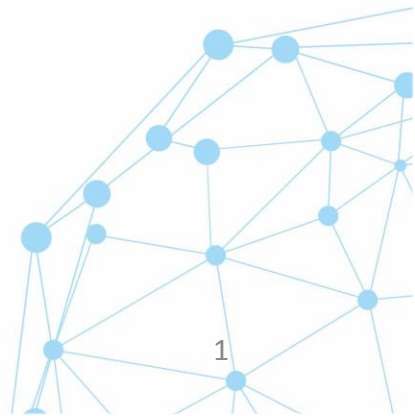*Patient Centricity and Integrated Quality Management*

February 27, 2020

Development of a Standard for Assessing and Improving Quality Culture

Presenter: Susan Schniepp, PDA Chair-Elect and Member of PDA's Quality Culture Team

Topics

1. Background
2. Regulatory Expectations
3. Why Quality Culture is Important
4. Understanding Behaviors vs. Attributes
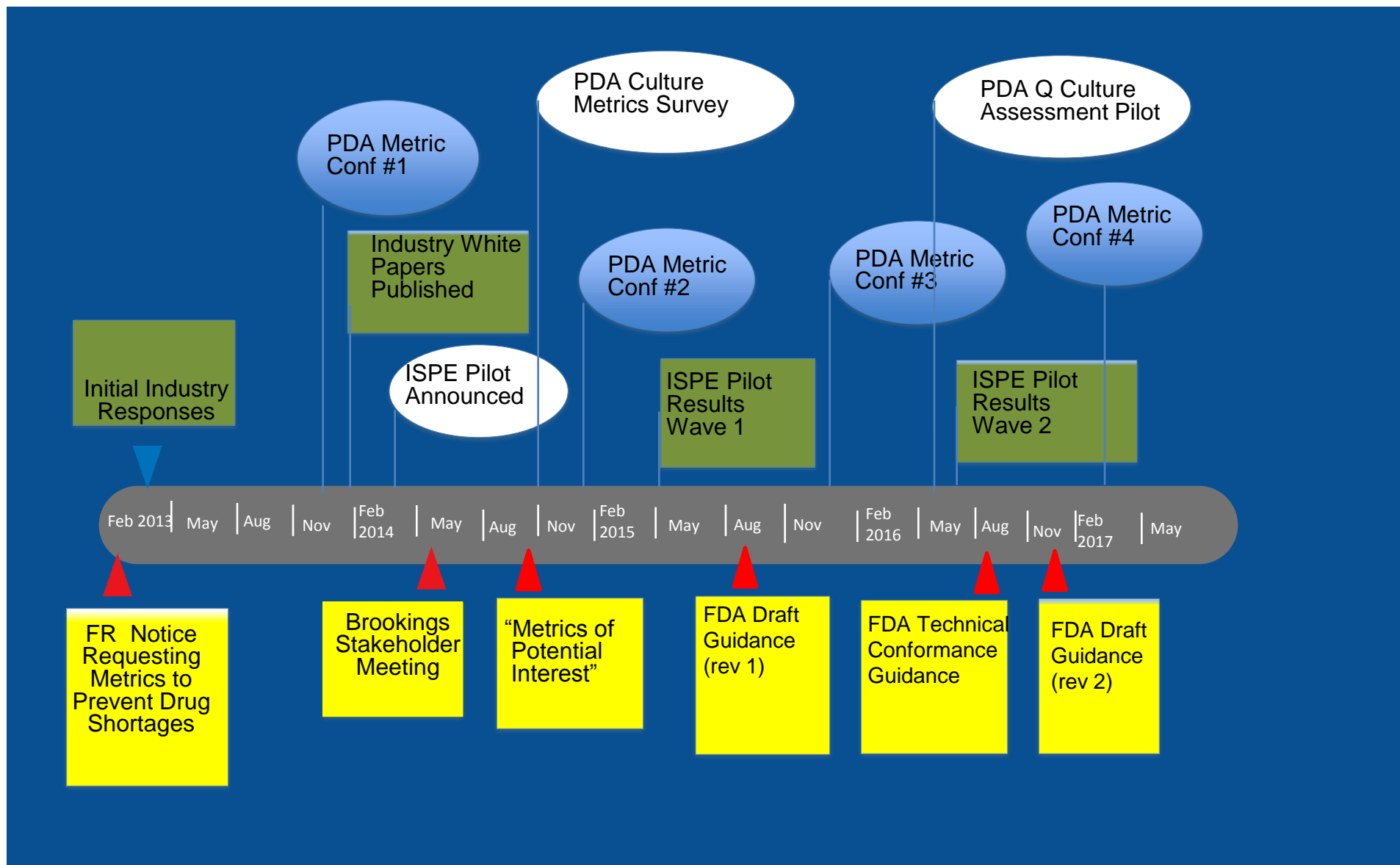5. PDA's Culture Journey
6. ANSI Standard
7. Acknowledgements

Quality Culture Transformation Resources
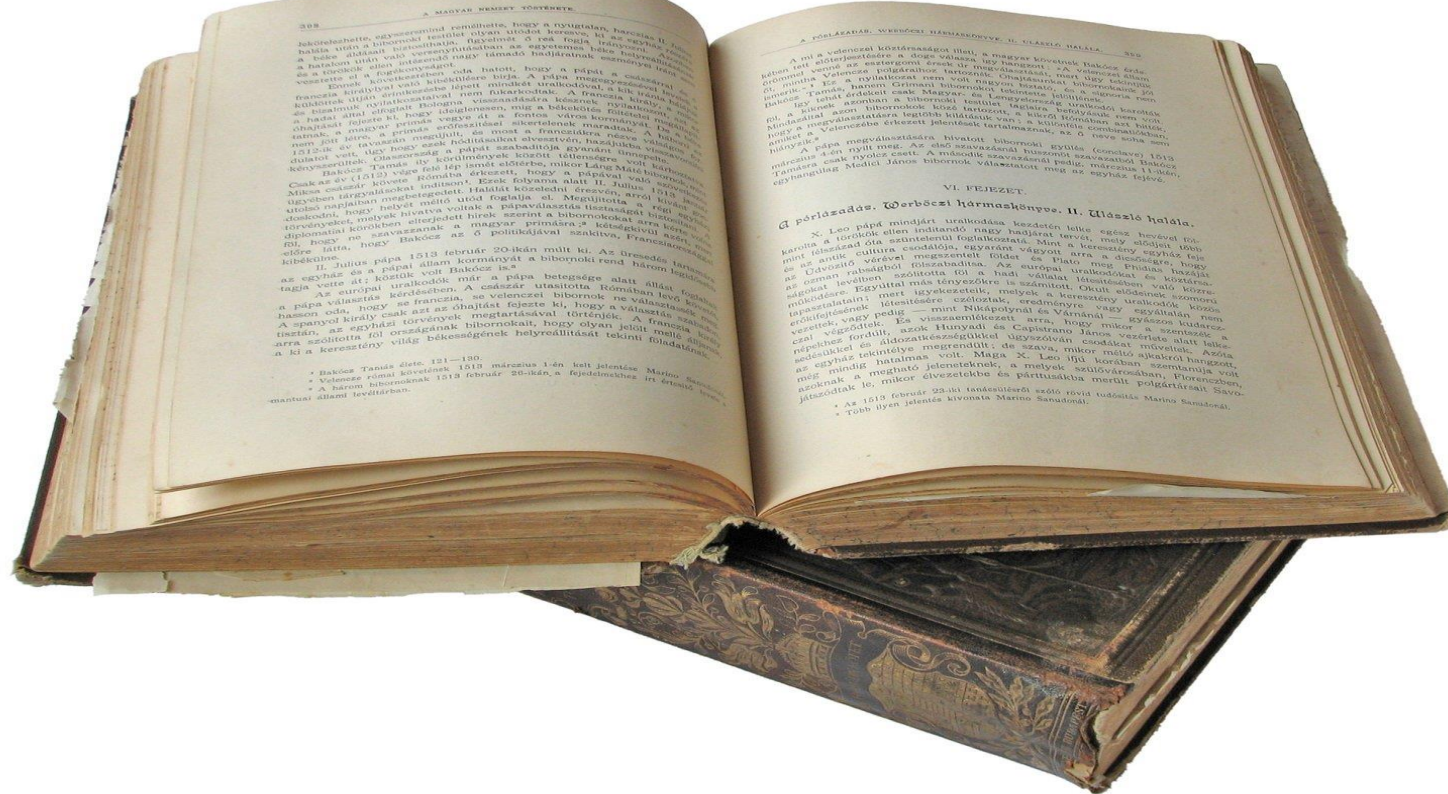
A maximally efficient, agile, flexible, pharmaceutical manufacturing sector that reliably produces high quality drug products <u>without extensive regulatory oversight</u>.

Janet Woodcock,FDA,Center for Drug Evaluation and Research October 5,200

PDA's Metrics Journey

PDA Metric Conf #1

PDA Culture Metrics Survey

PDA Q Culture Assessment Pilot

PDA Metric Conf #4

Industry White Papers Published

PDA Metric Conf #2

PDA Metric Conf #3

Initial Industry Responses

ISPE Pilot Announced

ISPE Pilot Results Wave 1

ISPE Pilot Results Wave 2

Feb 2013 | May | Aug | Nov | Feb 2014 | May | Aug | Nov | Feb 2015 | May | Aug | Nov | Feb 2016 | May | Aug | Nov | Feb 2017 | May

FR Notice Requesting Metrics to Prevent Drug Shortages

Brookings Stakeholder Meeting

"Metrics of Potential Interest"

FDA Draft Guidance (rev 1)

FDA Technical Conformance Guidance

FDA Draft Guidance (rev 2)

PDA's Metrics Journey (cont')

Optional Proposed Metrics - 2015

- Measuring Quality Culture

- Measuring Senior Management Engagement
  - CAPA Effectiveness
  - Process Capability/Performance

Lessons Learned

- Metrics is a very complex topic, fraught with unintended consequences.
- Trending is most important
- Optimizing a metric program takes time to evolve
- **Metrics has to be combined with a strong Quality Culture to be meaningful**
- Focusing on a metric can compromise its utility
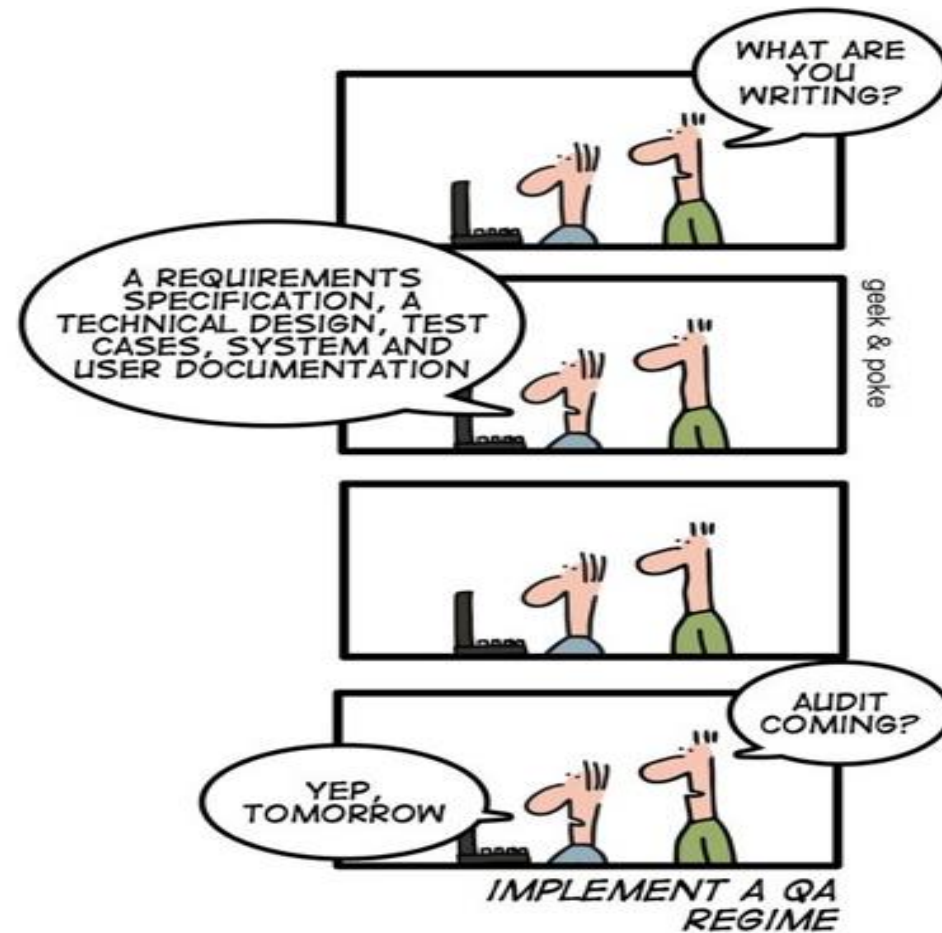- Finding forward looking metrics is very difficult

PDA Metric Task Force

- Steven Mendivil
- Denyse Baker
- Cylia Chen-Ooi
- Veronique Davoust
- Marci Goldfinger
- Robert Kieffer
- Shin-ichiro Mohri
- Marty Nealey

- Pritesh Patel
- Edwin Rivera-Martinez
- Anil Sawant
- Siegfried Schmitt
- Susan Schniepp
- Lorraine Thompson
- Glenn Wright

Regulatory Expectations

PIC/S: Good Practices for Data Management and Integrity in Regulated GMP/GDP Environments

- 6.3 <u>Quality Culture</u>
  - Management should aim to create a work environment (i.e. quality culture) that is transparent and open, one in which personnel are encouraged to freely communicate failures and mistakes. Organisational reporting structure should permit the information flow between personnel at all levels.

MHRA 'GXP' Data Integrity Guidance and Definitions

3. The principles of data integrity

    3.1 The organisation needs to take responsibility for the systems used and the data they generate. The organisational culture should ensure data is complete, consistent and accurate in all its forms, i.e. paper and electronic.

    3.3 The impact of organisational culture, the behaviour driven by performance indicators, objectives and senior management behaviour on the success of data governance measures should not be underestimated. The data governance policy (or equivalent) should be endorsed at the highest levels of the organisation.

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World Health Organization: Guidance on good data and record management practices

1. Introduction

    1.4 Examples of controls that may require development and strengthening to ensure good data management strategies include, but are not limited to:

- adoption of a quality culture within the company that encourages personnel to be transparent about failures so that management has an accurate understanding of risks and can then provide the necessary resources to achieve expectations and meet data quality standards:

12

World Health Organization: Guidance on good data and record management practices

4. Principles

    4.7 **Quality culture.** Management, with the support of the quality unit, should establish and maintain a working environment that minimizes the risk of non-compliant records and erroneous records and data. An essential element of the quality culture is the transparent and open reporting of deviations, errors, omissions and aberrant results at all levels of the organization, irrespective of hierarchy. Steps should be taken to prevent, and to detect and correct weaknesses in systems and procedures that may lead to data errors so as to continually improve the robustness of scientific decision-making within the organization. Senior management should actively discourage any management practices that might reasonably be expected to inhibit the active and complete reporting of such issues, for example, hierarchical constraints and blame cultures.

Warning Letters Citing Data Integrity Deficiencies				
	FY2013	FY2014	FY2015	FY2016
Total warning letters	38	22	19	46
US sites with DI deficiencies	0% (0 of 13)	0% (0 of 4)	33% (1 of 3)	73% (8 of 11)
Outside US sites with DI deficiencies	40% (10 of 25)	67% (12 of 18)	81% (13 of 16)	81% (29 of 35)
Total number of warning letters citing DI deficiencies	26% (10 of 48)	55% (12 of 22)	74% (14 of 19)	79% (37 of 46)

Office of Manufacturing Quality CY17 Warning Letters

Note: Compounding warning letters excluded.

Legend: Other, India, China, US

*Through September 1, 2017. Compounding warning letters are not included.

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Industry Changes

Emergence of Generic Industry

Emergence of Biosimilars

Emergence of Virtual Companies

Emergence of CMOs

Emergence of Compounding Pharmacies & 503b Outsourcing Facilities

Institutional Knowledge Lost through M&A
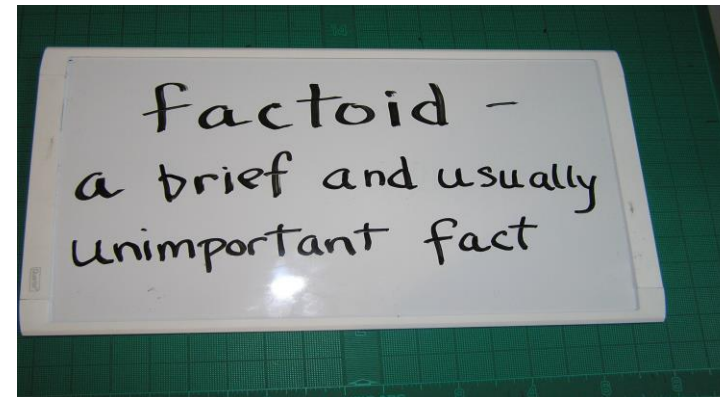
Emergence of Information Technology

Between 2005 and 2016 there were ≈225 Warning Letters Issued for "Data Integrity"

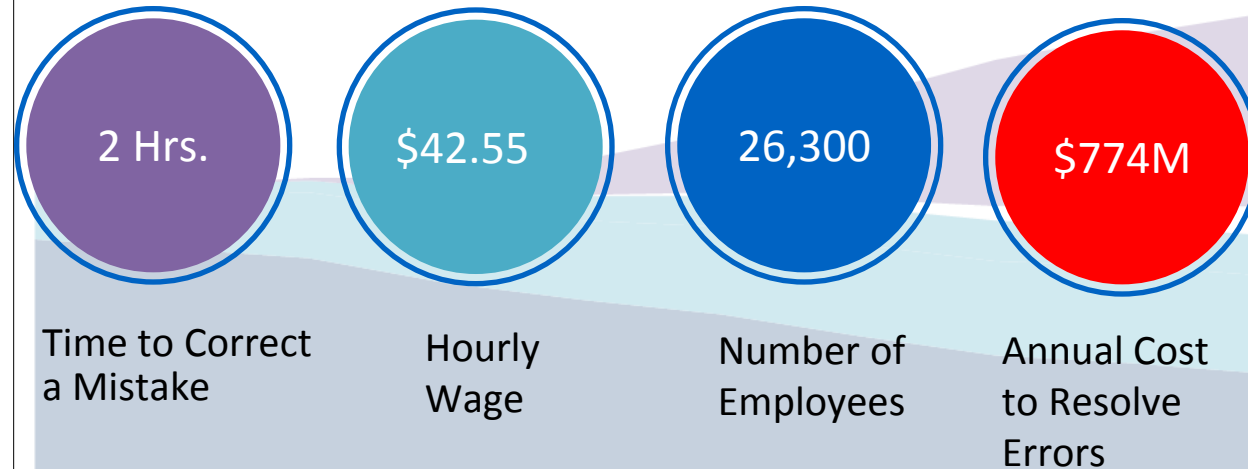In 2002 at the International GMP Symposium Issues of Concern Were:
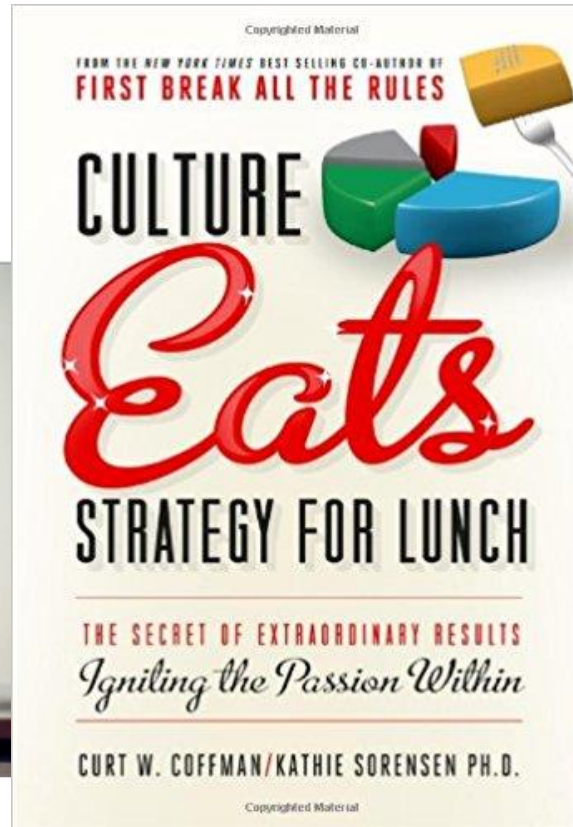
Improper documentation

Lack of Thorough Investigations
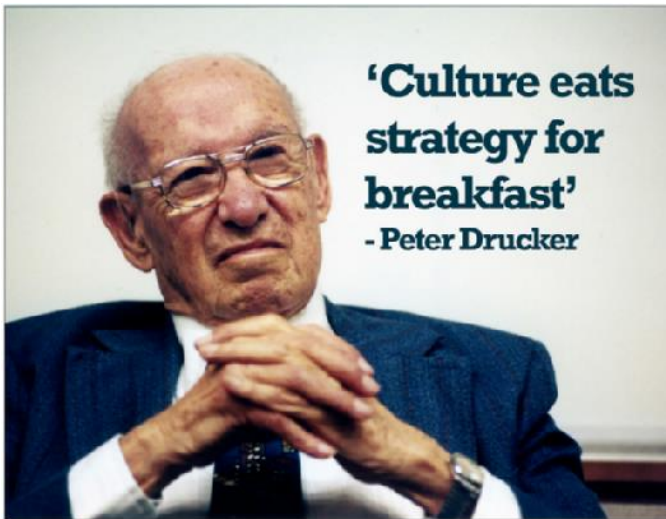
Insufficient Training

factoid –
a brief and usually
unimportant fact

Business Benefits of a Quality Culture

2 Hrs.	$42.55	26,300	$774M
Time to Correct a Mistake	Hourly Wage	Number of Employees	Annual Cost to Resolve Errors

For every 5,000 employees, moving from the bottom to the top quintile would save a company $67 million annually
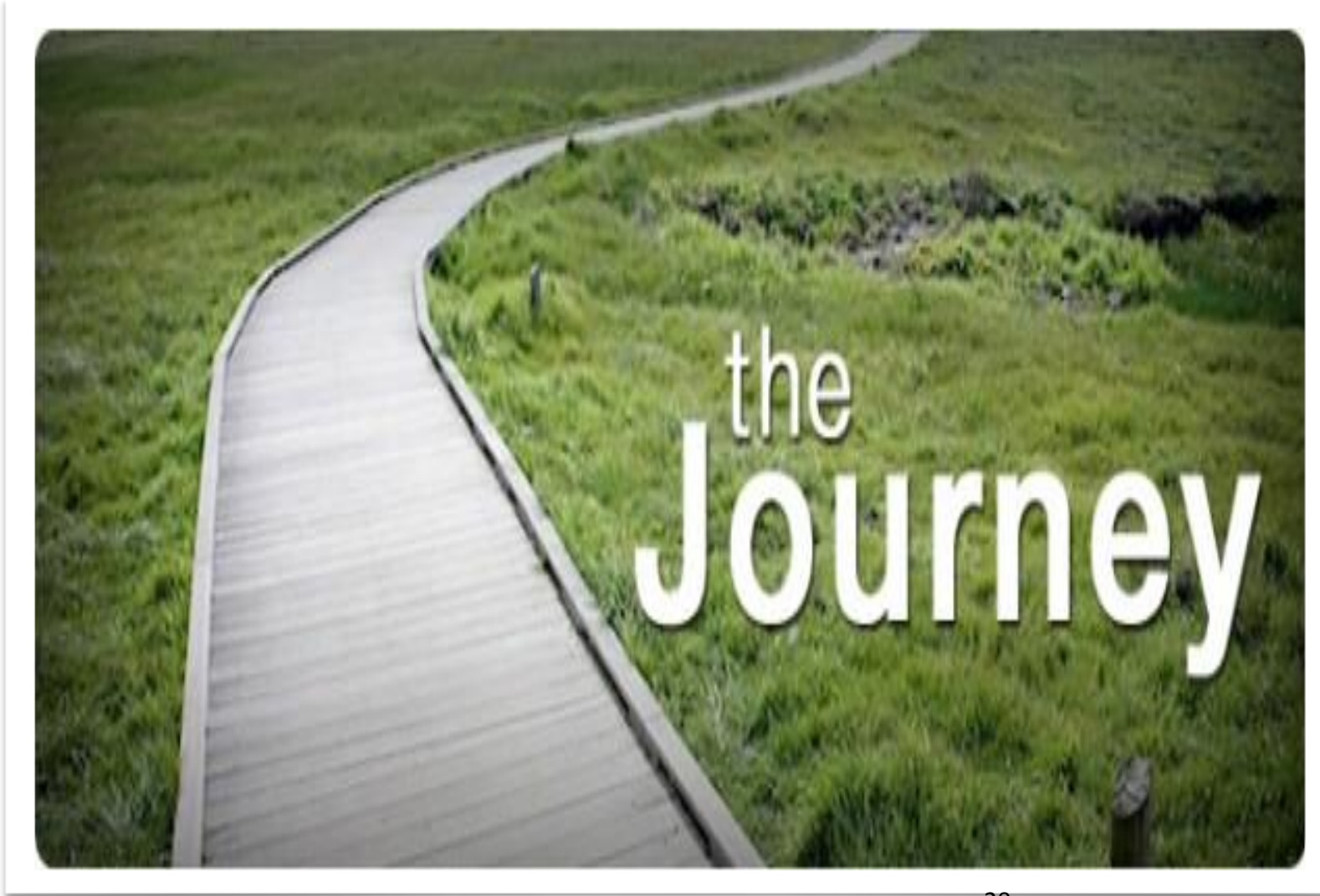
Harvard Business Review April 2014 "Creating a Culture of Quality"
CEB (Corporate Executive Board) Results of Two Years of Research
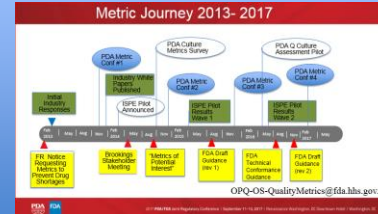
2000's The Importance of Culture was Realized

'Culture eats strategy for breakfast'
- Peter Drucker

FROM THE *NEW YORK TIMES* BEST SELLING CO-AUTHOR OF
FIRST BREAK ALL THE RULES

CULTURE Eats STRATEGY FOR LUNCH

THE SECRET OF EXTRAORDINARY RESULTS
Igniting the Passion Within

CURT W. COFFMAN/KATHIE SORENSEN PH.D.

CULTURE EATS STRATEGY FOR BREAKFAST, OPERATIONAL EXCELLENCE FOR LUNCH AND EVERYTHING ELSE FOR DINNER.

Behappy.me

Connecting People, Science and Regulation®

Response to FDA Metrics
2013-2014

Hypothesis to measure Culture

Quality Culture Pilot Program
2016-2017

Can I compare with other sites?

Quality Culture Survey
2014-2015
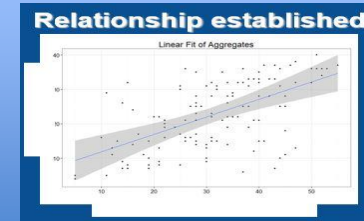
Is there a correlation between behavior and attributes?

Quality Culture Model
2015-2016
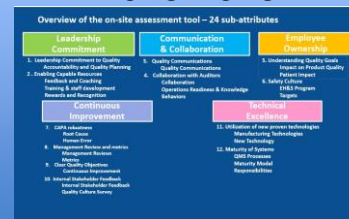
What attributes are most important?

What is quality culture?

"True culture of quality" is an environment in which employees not only follow quality guidelines but also consistently **see** others taking quality-focused actions, **hear** others talking about quality, and **feel** quality all around them (Harvard Business Review)

Culture is the behaviors and beliefs characteristic of a particular social group. It indicate what is important to the companies, thus, impacts their decision making

Quality culture is the root cause of many of quality problems, such as data integrity

Many of the things you can count, don't count, many of the things you can't count really counts – Albert Einstein

## WARNING SIGNS

- The CEO and other senior executives rarely discuss quality—let alone performance against quality objectives.

- The company's quality vision is either non-existent or has minimal linkage to business strategy.

- Managers throughout the organization either fail to consistently emphasize quality or are resistant to quality initiatives.

- The organization has few if any feedback loops for continuous improvement of processes.

- The company lacks formal mechanisms for collecting and analyzing customer feedback.

- Metrics used for performance evaluation feature little-to-no mention of quality goals.

- Employees are not familiar with the company's quality vision and values—or perhaps worse, view them as mere slogans.

- Training and development do not emphasize quality.

- New hires are not formally introduced to the organization's quality vision and values.

- The organization experiences frequent, though often minor, setbacks owing to inconsistent quality.
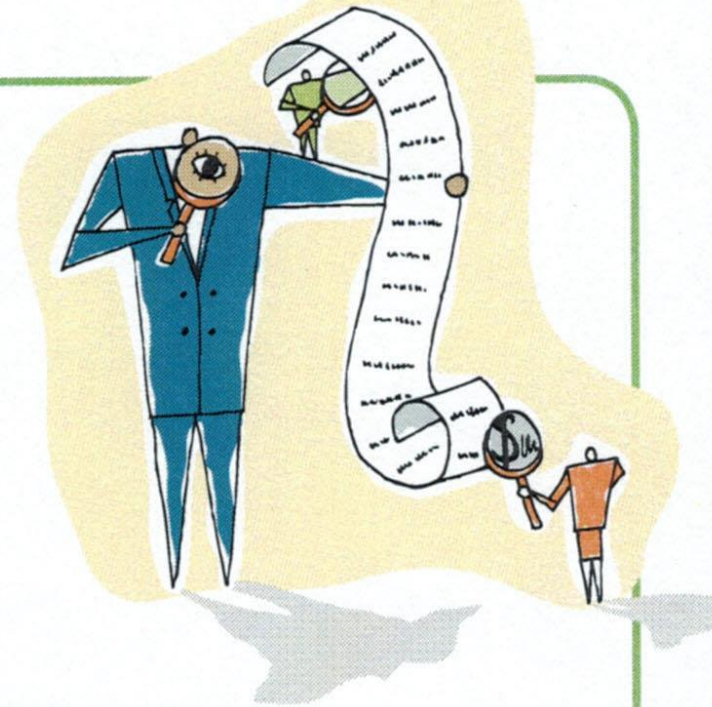
Vision / Mission:

   Promote Quality Culture, its understanding, assessment and improvement within the Pharmaceutical / Biopharmaceutical Industry by providing tools and knowledge to enable continuous improvement. The ideal state is to ensure a quality mindset and behaviors are imbedded into the daily work of all functions resulting in positive patient outcomes.

Is there a set of Mature Quality Attributes that are a surrogate for Quality Culture Behaviors?

1. Is there a relationship between Quality Culture Behavior scores and Mature Quality Attribute scores?

2. Which Mature Quality Attributes relates to Quality Culture behavior?
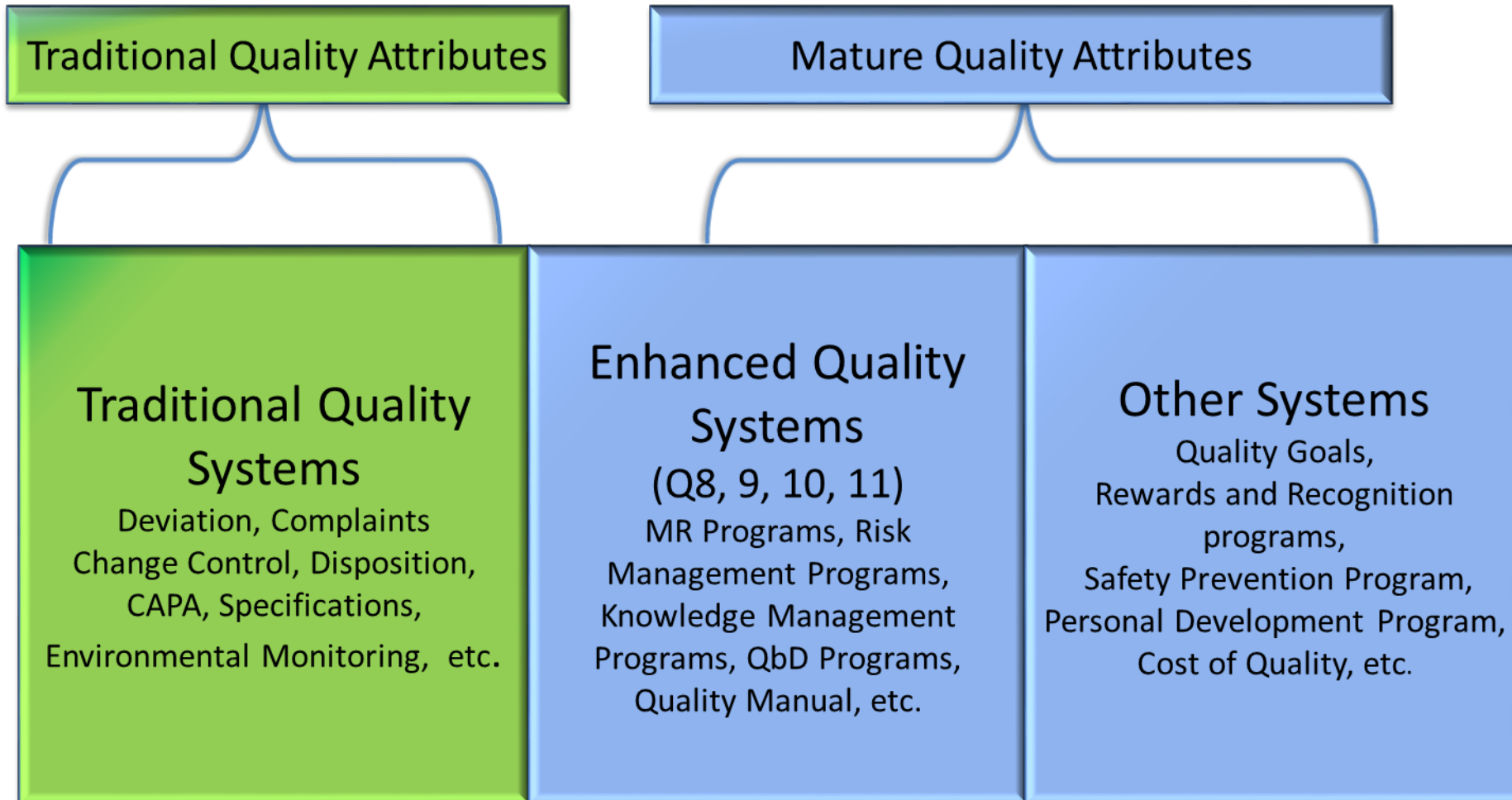

Creating a Road Map

Quality Attributes:

- Objective characteristics of a quality system
- Can be verified
- A tangible program or system
- Can be verified

Examples include:

- Deviations reporting
- Change control system
- CAPA system
- Complaints management system
- Environmental monitoring program

Traditional Quality Attributes

Mature Quality Attributes

Traditional Quality Systems
Deviation, Complaints
Change Control, Disposition,
CAPA, Specifications,
Environmental Monitoring, etc.

Enhanced Quality Systems (Q8, 9, 10, 11)
MR Programs, Risk Management Programs, Knowledge Management Programs, QbD Programs, Quality Manual, etc.

Other Systems
Quality Goals, Rewards and Recognition programs, Safety Prevention Program, Personal Development Program, Cost of Quality, etc.

Seven Areas of Questions

1. Prevention Programs
2. Quality Management and Issue Escalation
3. Training and Personnel Development
4. Quality System Management
5. People and Communication
6. Continuous Improvement
7. Site Metric Reporting

These 7 areas identified 55 Mature Quality Attributes

Quality Behaviors:

- Actions that need to observed or experienced
- Difficult to quantify or audit
- Are the characteristics of the culture

Examples include:

- Communication & Transparency
- Rewards and Recognition
- Engagement
- Cross Functional Vision

Quality Culture Behavior
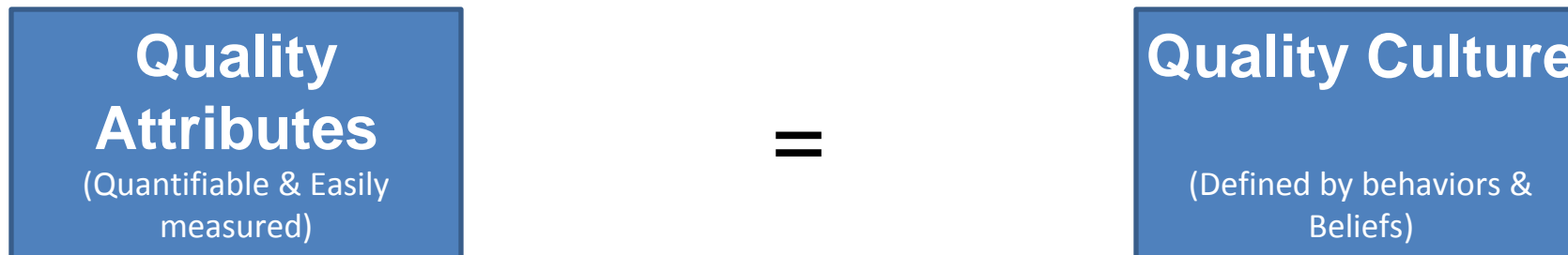
Seven Areas of Behavior Questions

1. Communication & Transparency
2. Commitment & Engagement
3. Technical Excellence
4. Standardization of Criteria or Requirements
5. Cross Functional Vision
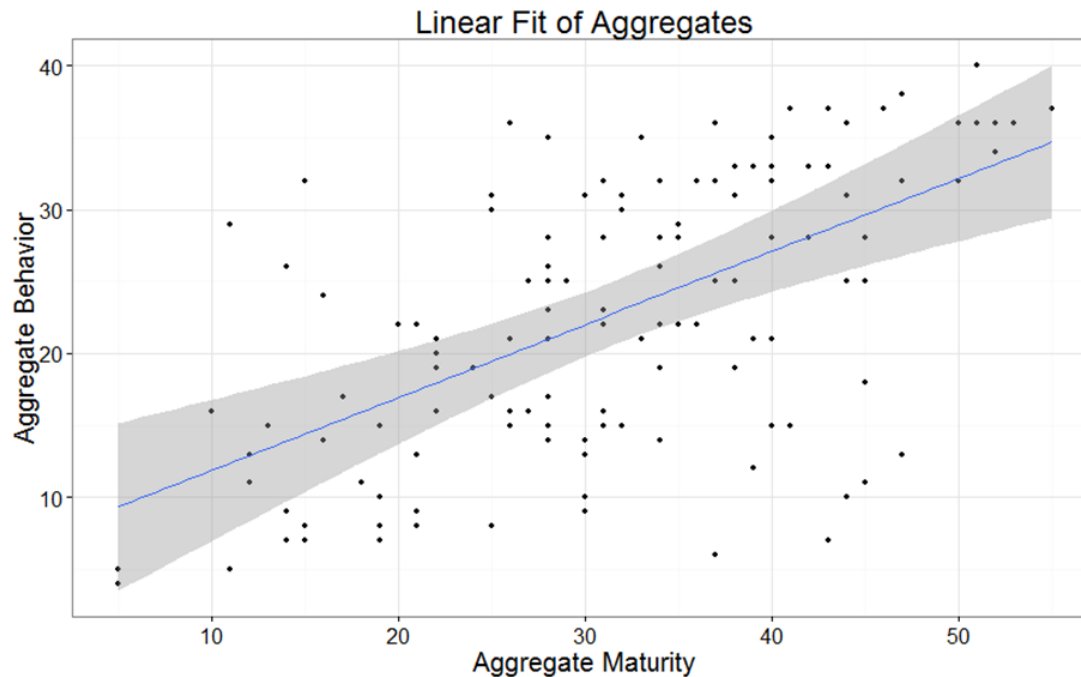6. Rewards and Recognition
7. Speak Up for Quality Culture

These 7 areas identify 42 specific behaviors

IF....

Quality Attributes (Quantifiable & Easily measured)	=	**Quality Behaviors** (Difficult to measure, often need to be observed)	=	**Quality Culture** (Defined by behaviors & Beliefs)

Then…

Quality Attributes (Quantifiable & Easily measured)	=	**Quality Culture** (Defined by behaviors & Beliefs)

Linear Fit of Aggregates

PDA Quality Culture Survey analysis
http://journal.pda.org/content/69/5/631.full.pdf+html?sid=1d68365b-c441-4c68-943f-eb0f39ce084e
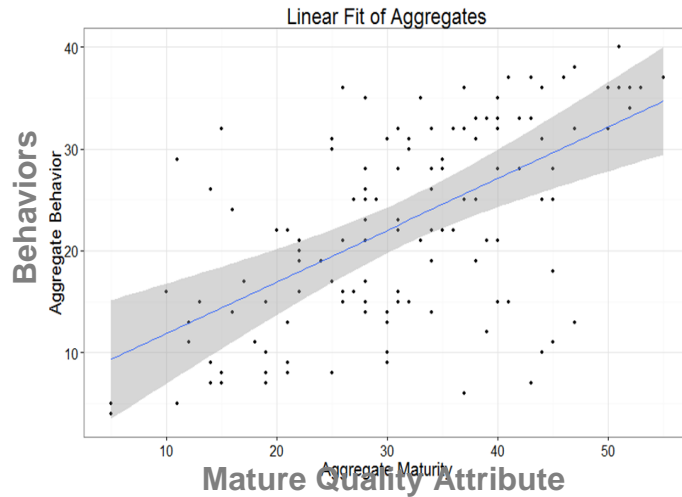
Higher MQA score the higher the behavioral score

Given this is a Social Science Analysis, this is a strong relationship

Yes! There is a relationship between Quality Culture Behavior and Mature Quality Attribute

St.Gallen confirms PDA's Quality Culture Survey outcome
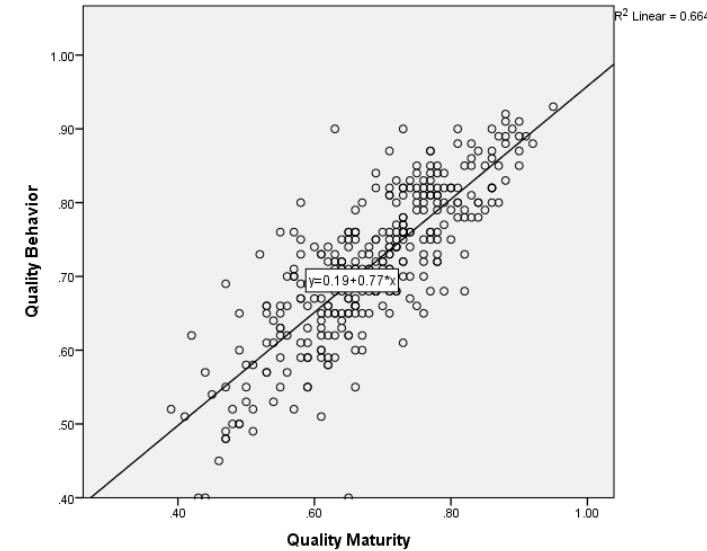
PDA Survey Analysis 2014

St.Gallen Analysis 2017

$R^2 = 0.34$ → $R^2 = 0.66$

- 326 pharmaceutical sites of different size and focus within St.Gallen database confirm PDA

Most impactful attributes identified

1. Participation at conferences to stay current
2. Collecting Error Prevention Metrics
3. Management Communication that Quality is Everyone's Responsibility
4. Utilization of new proven technologies
5. Clear performance criteria for feedback and coaching
6. EH&S Environmental Program with trained staff (risk assessments, emission controls, spill prevention and response)
7. Site has formal quality improvement objectives and targets
8. Quality topics included in at least half of "all hands" meetings
9. Collecting Management Review Metrics
10. Collecting Employee Turn Over Rate Metrics

11. Program to show how employee's specific goals contribute to overall quality goals
12. Program to measure, share and discuss product quality performance and improvement from shop floor to executive management.
13. Continuous Improvement Program / Plans with active support of CEO and Corp Management of QMS
14. Program that establishes quality system maturity model and action plan and tracking to measure progress
15. Internal survey measuring a company/ site quality culture

Voted by ~225 Conference Participants, Dec 2014

PDA tool was developed with five categories

Leadership Commitment

1. **Accountability and Quality Planning**
   Accountability & Quality Planning

2. **Enabling Capable Resources**
   Feedback & Staff Development
   Training
   Rewards and Recognition

Communication & Collaboration

3. **Quality Communications**
   Quality Communications

4. **Communication and Collaboration**
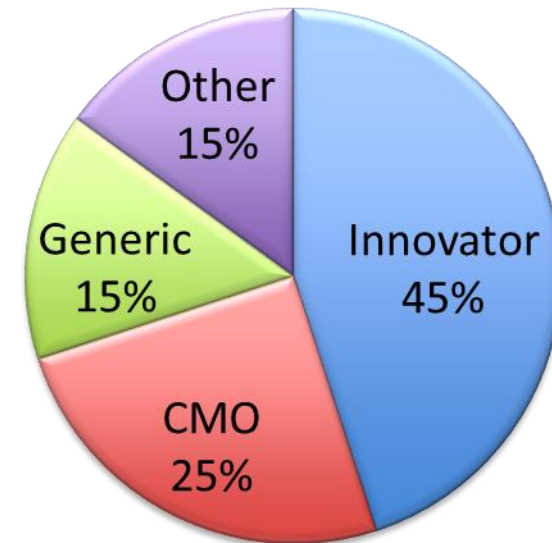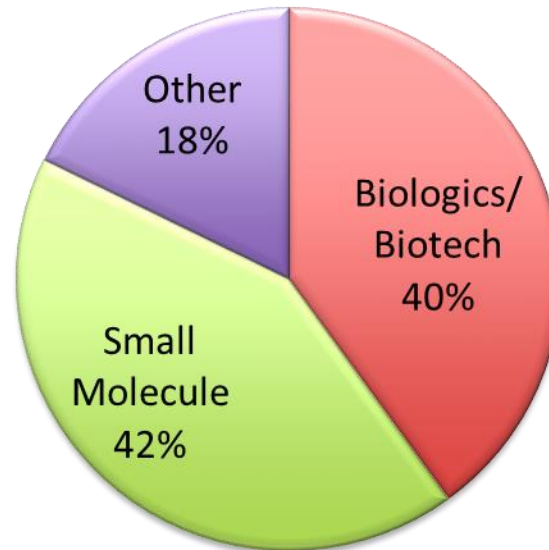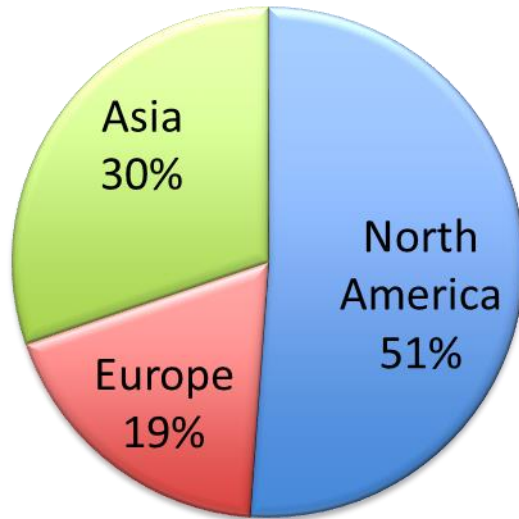   Operations Readiness & Knowledge

Employee Ownership and Engagement

5. **Understanding Quality Goals**
   Impact on Product Quality
   Patient Impact

6. **Staff Empowerment and Engagement**
   Process Ownership & Engagement
   Safety Program

Continuous Improvement

7. **CAPA robustness**
   Root Cause
   Human Error

8. **Management Review and metrics**
   Management Reviews
   Metrics

9. **Clear Quality Objectives and Targets**
   Continuous Improvement

10. **Internal Stakeholder Feedback**
    Internal Stakeholder Feedback
    Quality Culture Survey

Technical Excellence

11. **Utilization of New Technologies**
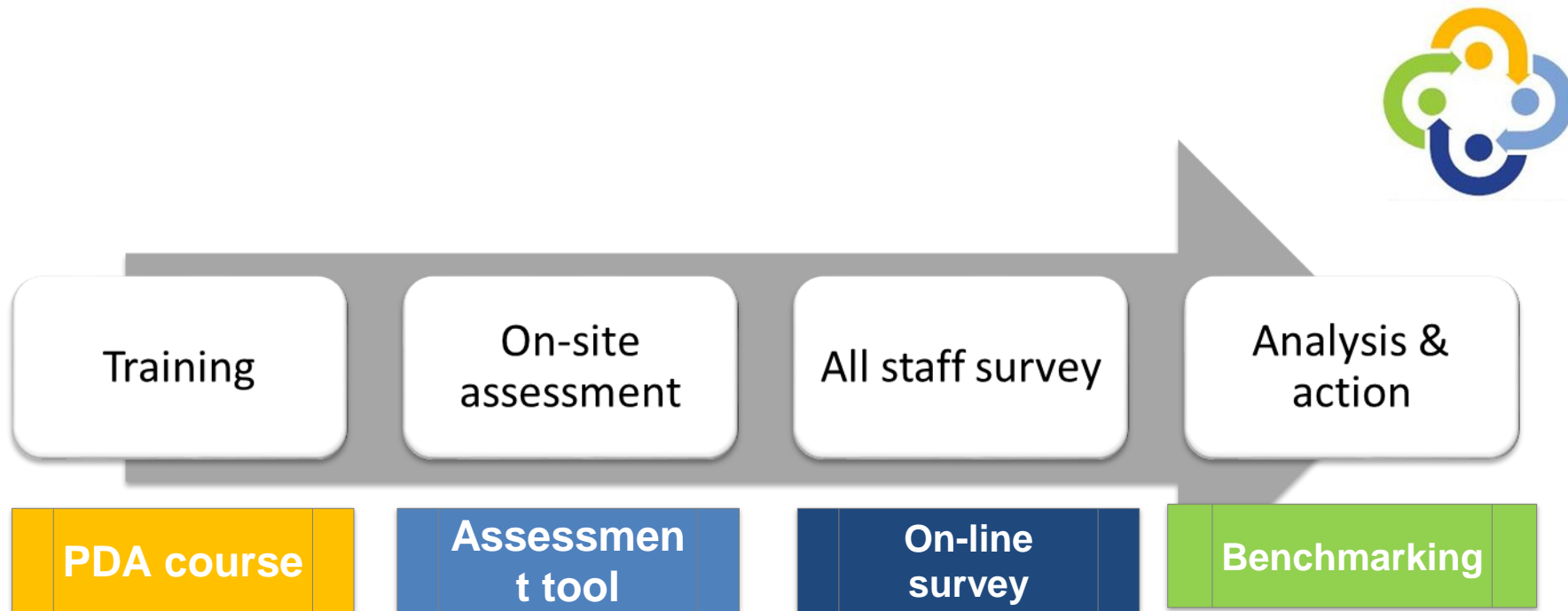   Manufacturing Technologies

12. **Maturity of Systems**
    QMS Processes
    Business Conduct
    Quality Risk Management

Total of 75 assessors trained; 9000+ survey respondents

What did the pilot involve?

Training   On-site assessment   All staff survey   Analysis & action

PDA course   **Assessment tool**   **On-line survey**   **Benchmarking**
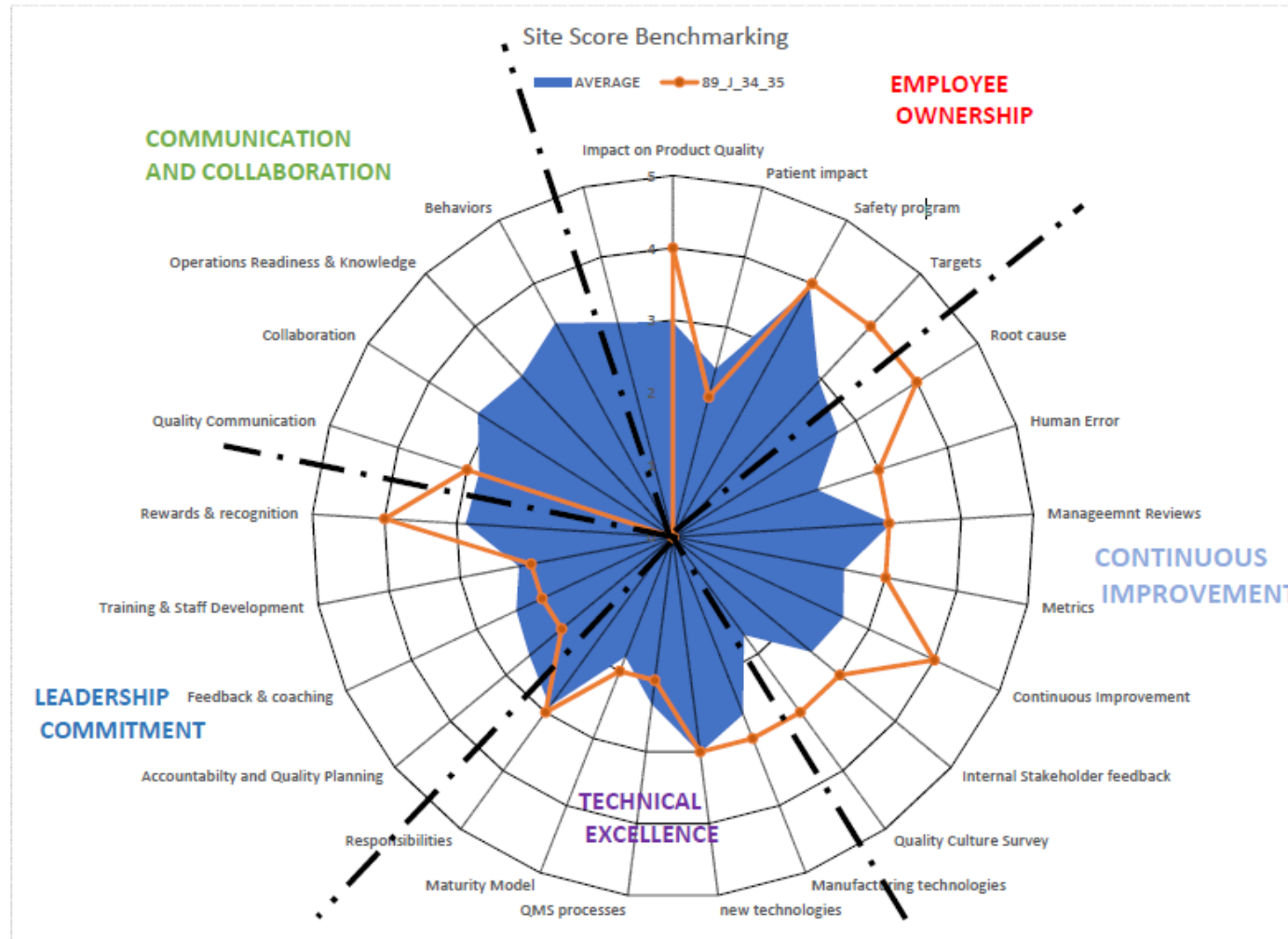
Copyright PDA 2017 for Exclusive Use of Culture Pilot Participants

Positive feedbacks

- Clear framework and scoring method
- Drive effective discussion with site leadership
- "Best PDA training"
- In-person discussions provides more value in understanding the culture at the site (vs. only a survey)
- Reliable way to help select partners and CMOs

Challenges

- Assessment is most effective with a different mindset and approach
- Pre-work needed to gain efficiency

☑ Was the training effective?

☑ Can sites be differentiated?

☑ Was the tool user-friendly?

☑ Were the assessment results useful for discussion with site management?

Over 100 regulators from MHRA and USFDA have been trained on PDA's Culture Assessment Tool

"[We] can apply the Quality Culture Attributes to improve how we assess firms in non-compliance context"

"As industry becomes aware and comfortable with this tool… it can be a powerful tool for evaluating CMOs and business partners."

"Industry can use the PDA tool as part of internal/self-assessment for improvement of Quality Systems."

"Industry could use the PDA tool to be more open with regulators on quality culture."

"I will consider quality culture when reviewing data from industry."

"Nice to differentiate quality Culture from Quality Systems and emphasize the importance of what we make relative to what we do."

"This course does help identify quality culture issues in a company. This may help [us] to evaluate the quality of a pharmaceutical company."

ANSI Standard

Title of Proposed Standard:
Quality Culture Assessment Tool

Stakeholder Category being represented:

    X **General Interest**

    X **Producer Interest members**

    X **User Interest members**

    X **Regulatory Interest members**

Project Description:

The U.S. FDA continues to focus on the use of quality metrics to modernize pharmaceutical quality systems and advance innovation. In a recently published [document](#), FDA has called for routine assessment and management oversight of quality culture. In addition, MHRA, PIC/S and the WHO have all issued guidance on data integrity that specifically call for companies to address the issue of quality culture. There is currently no agreed-upon standardized way for companies to effectively measure their quality culture. PDA has already designed a comprehensive *Quality Culture Assessment Tool and Training*, designed to guide companies to a better understanding of quality culture, how to assess it, and what actions to take to improve it. The tool helps a company effectively collect verifiable data that will help them to assess their culture at all levels of their organization. The tool allows the company to facilitate positive culture changes and continuous improvement within their organization. This tool will serve as the basis for the development of a consensus standard to guide quality assessment and facilitate benchmarking both within and across organizations.

PDA (Parenteral Drug Association)

Contact: Christine Alston-Roberts, (301)-656-5900-, roberts@pda.org

Bethesda Towers, 4350 East-West Highway, Bethesda, MD 20814

New Standard

BSR/PDA Standard 06-201x, Quality Culture Assessment Tool (new standard)

Stakeholders: Quality assurance, quality control, quality engineering, operations, production, manufacturing, general interest, regulatory interest members.

Project Need: Provide a data-driven assessment approach to allow companies to effectively measure quality culture and its importance in providing high-quality medicinal products to patients.

A comprehensive Quality Culture Assessment Tool and Training, designed to guide companies to a better understanding of quality culture, how to assess it, and what actions to take to improve it. The tool helps a company effectively collect verifiable data that will help them to assess their culture at all levels of their organization. The tool allows the company to facilitate positive culture changes and continuous improvement within their organization.

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PDA® Standards Development: Call for Volunteers:

Standard 06-201x, Quality Culture Assessment Tool (new standard).

PDA is very pleased to announce the launch of the Parenteral Drug Association's sixth standard!

We are seeking volunteer participants to assist in developing, writing, and fine tuning the following proposal:

Standard 06-201x, Quality Culture Assessment Tool (new standard).
A comprehensive Quality Culture Assessment Tool and Training, designed to guide companies to a better understanding of quality culture, how to assess it, and what actions to take to improve it. The tool helps a company effectively collect verifiable data that will help them to assess their culture at all levels of their organization. The tool allows the company to facilitate positive culture changes and continuous improvement within their organization.

This proposed American National Standard (ANS) was presented by Susan Schniepp, Distinguished Fellow with Regulatory Compliance Associates.

Those individuals involved in Quality Assurance, Quality Control, Quality Engineering, Operations, Production, and

Manufacturing, Regulatory, and General Interest are needed.

Nominations/Volunteers to serve as a member of the technical team (consensus body) must have some subject matter expertise, and willing to help

write/contribute to this standard. Applicants should apply by contacting the PDA Standards Manager at standards@pda.org.

The deadline to submit notification of interest in serving on the consensus body is **January 14, 2020.**
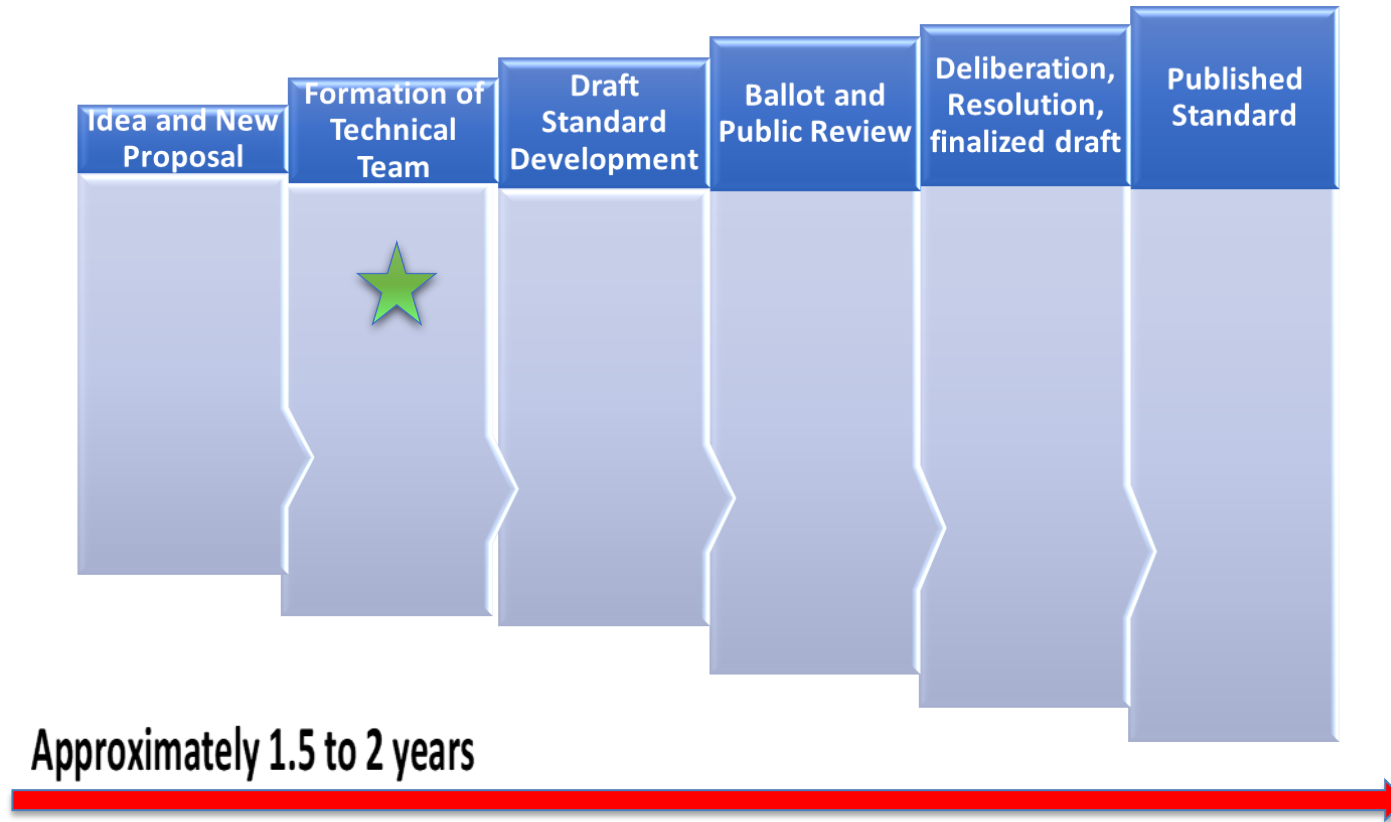
PDA Quality Culture Team

Cylia Chen (Amgen) – team lead

Steve Mendivil (Amgen)

Machelle Eppler (Patheon)

Pritesh Patel (Novartis)

Sue Schniepp (Consultant)

Chuck Bornhoeft (Upsher-Smith)

Joerg Gampfer (Hovione)

Dixie Webster (Allergan)

Tara Gooen-Bizjak (FDA)

Gerald Heddell (MHRA)

Matija Gabrovsek (Novartis)

Brianna Peterson (BI)

Jan Paul Zonnenberg (PwC)

Sandra Lueken (AstraZeneca)

Anne Eickhoff (GSK)

Rick Burdick (Consultant)

Bob Kieffer (Consultant)

David Leuck (Patheon)

Denyse Baker (PDA)
Rich Levy (PDA)
David Talmage (PDA)

"Quality is always fashionable."

Boy George (George Alan O'Dowd), Lead Singer of Culture Club
1961 - present