FDA Quality Metrics

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Johnson & Johnson

13 November 2017

Abstract

Quality Metrics are used throughout the healthcare industry to monitor systems and processes and drive continuous improvement efforts. FDA issued draft guidance documents for industry's submission of quality metrics in 2015 and 2016. This has sparked discussion and debate as to whether it is possible to standardize definitions across such a diverse industry.

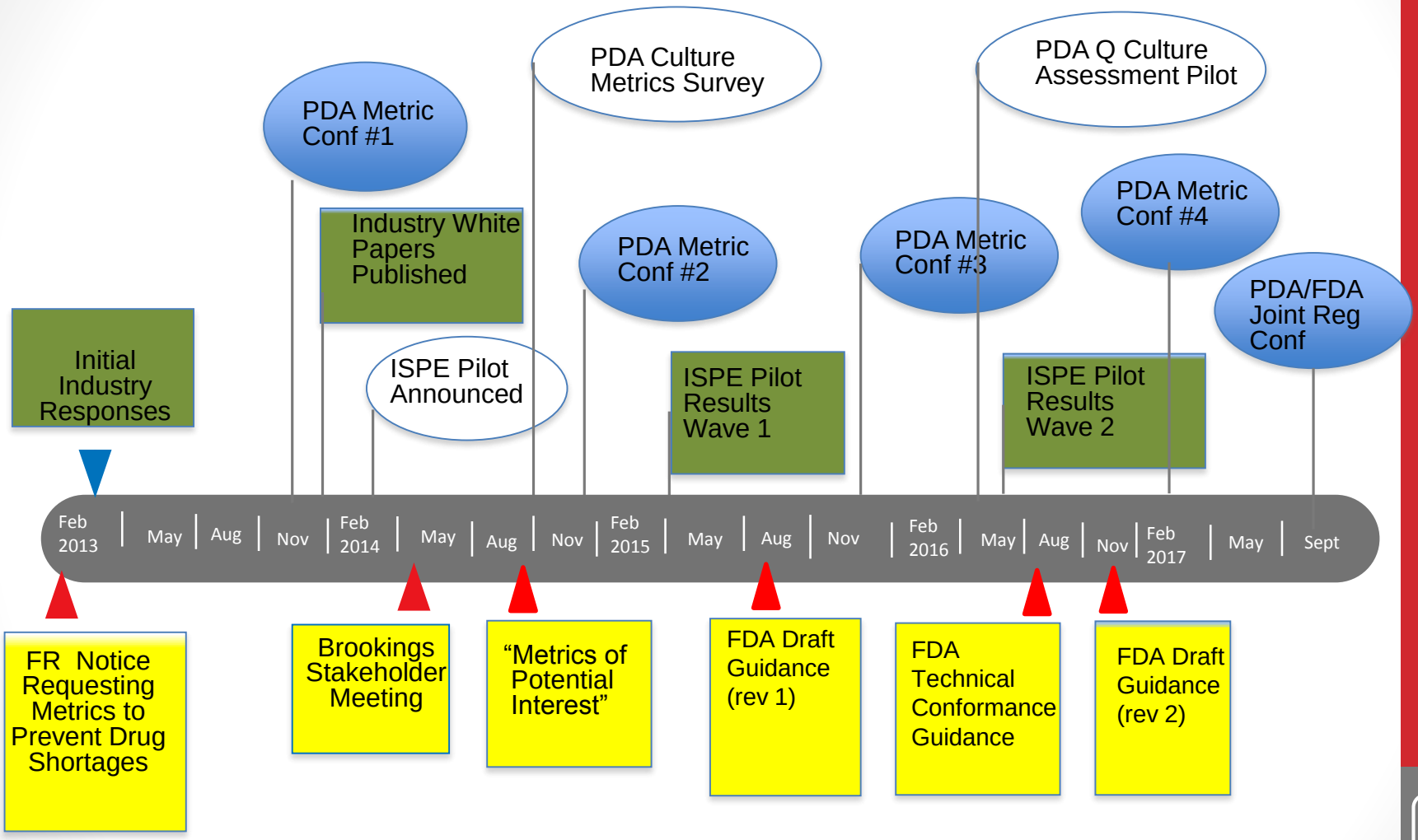
This presentation provides an overview of the evolution of these guidance documents, along with a review of the data elements in the most recent draft guidance and the metrics FDA intends to calculate. Potential next steps will be discussed following FDA's announcement at the September PDA/FDA conference that voluntary reporting will not commence in January 2018 as originally planned.

Fun with Metrics!

FDA Goals for Quality Metrics

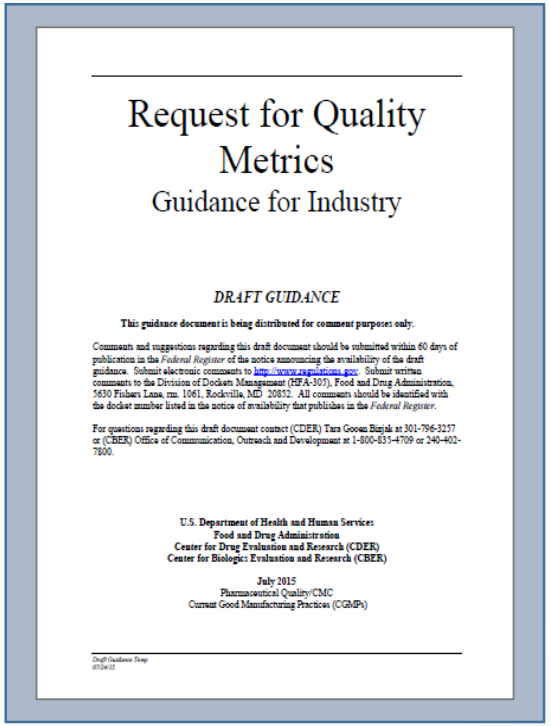
- Promote responsibility & culture
- Identify situations
- Improve FDA's evaluation
- Improve inspection program
- Inspection scheduling

Metrics Journey 2013-2017



2015 FDA Draft Guidance

- Lot Acceptance Rate
- Product Quality Complaint Rate
- Invalidated OOS Rate
- Annual Product Review or Product Quality Review on Time Rate



Request for Quality Metrics

Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to http://www.regulations.gov. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document contact (CDER) Tara Goosen Binjak at 301-796-3237 or (CBER) Office of Communication, Outreach and Development at 1-800-835-4709 or 240-402-7800.

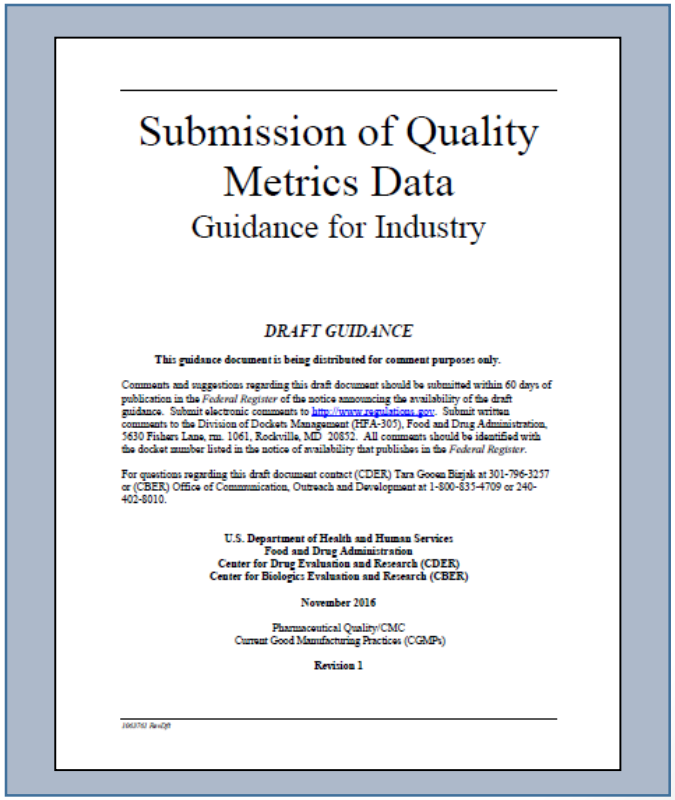
U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

July 2015
Pharmaceutical Quality/CMC
Current Good Manufacturing Practices (CGMPs)

Draft Guidance Temp
07/24/15

2016 FDA Draft Guidance

- Lot Acceptance Rate
- Product Quality Complaint Rate
- Invalidated OOS Rate



Submission of Quality Metrics Data

Guidance for Industry

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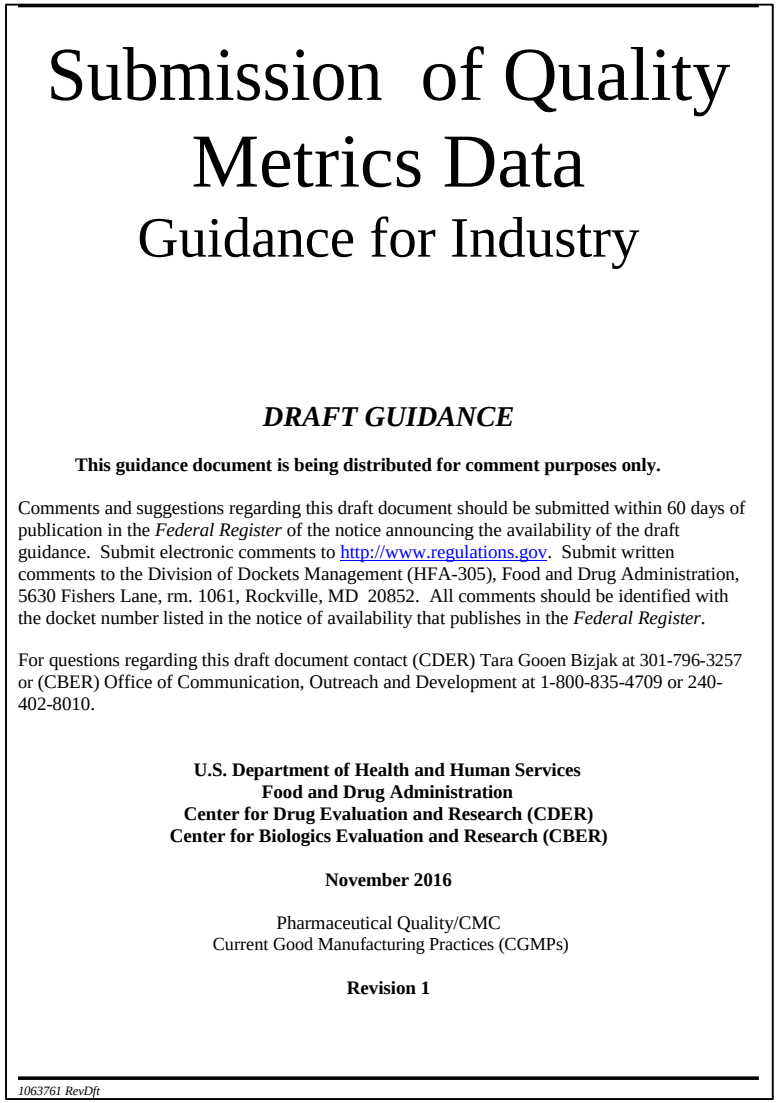
November 2016

Pharmaceutical Quality/CMC
Current Good Manufacturing Practices (CGMPs)

Revision 1

2016 FDA Draft Guidance



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November 2016

Pharmaceutical Quality/CMC
Current Good Manufacturing Practices (CGMPs)

Revision 1

1063761 RevDft

How FDA Intends to Use Quality Metrics

To focus the use of FDA resources on the areas of highest risk to public health (e.g. risk based inspection scheduling).

Specifically:

- Establish a signal detection program as one factor in identifying establishments and products that may pose significant risk to consumers.
- Identify situations in which there may be a risk of drug supply disruption
- Improve effectiveness of establishment inspections via risk based inspection approach
- Improve FDA's evaluation of drug manufacturing and control operations

Things to Know

- Scope: All drug products manufactured OR marketed in the US.

- Nov 2016 Draft Guidance: Establishes a voluntary pilot with FDA for data submission (by product or by site)
  - FDA planning to use results of pilot to move into rule-making

When Would Quality Data Submission Begin?

In the current Draft Guidance, FDA is asking for:

Voluntary product data reports

- In early 2018 (January – March)*
- Separate reports for API and Finished Drug
- Submission of data for calendar year 2017
  - 2017 annual data segmented by quarter

* **Paused 11 Sep 2017**

Docket Comments to Revised Draft Guidance (March 2017)

- 25 Submissions
  - 83 to first version of guidance
- 12 Associations
- 10 Individual Firms
- 1 Hospital Group
- 1 Academic Institution
- 1 Individual

FDA U.S. FOOD & DRUG ADMINISTRATION

Common Themes in Docket Responses

- Support for FDA objectives
- Acknowledgement that FDA listened and acted upon industry concerns in second draft
- Revised Draft doesn’t resolve all the issues
- Metrics commonly used by individual firms but challenges with standardized program
- Many questions on calculations, definitions, datasets

Key Points in PDA's Response

- Define success criteria for voluntary phase
- Q&A Document developed to clarify definitions
- Focus on metric/data trends rather than comparison of absolute values
- Ask FDA to advocate for harmonization efforts
- Recognition list of all voluntary participants

THE METRICS & DATA ELEMENTS

3 Quality Metrics To Be Calculated by FDA

(2016 FDA Draft Guidance)

	Metrics	Definition	
1	**Lot Acceptance Rate**	Measures robustness of commercial manufacturing process 	= the number of accepted lots in a timeframe divided by the number of lots started by the same covered establishment in the current reporting timeframe
2	**Product Quality Complaint Rate**	Measures voice of patient / customer 	= the number of product quality complaints received for the product divided by the total number of dosage units distributed in the reporting timeframe
3	**Invalidated Out of Spec Rate**	Measures robustness of Laboratory Operation 	= the number of OOS test results for lot release and long term stability testing invalidated by the covered establishment due to an aberration of the measurement process divided by the total number of lot release and long-term stability OOS in the current reporting timeframe

How these metrics have evolved

Lot Acceptance Rate

Russ Wesdyck, FDA **Dec 2013** (PDA Metrics Conference)	Batch Failure Rate
Brookings Quality Metrics Meeting, **May 2014**	Number of lots rejected / Number of lots attempted
Russ Wesdyck, FDA **Dec 2014** (PDA Metrics Conference)	= 1- (the number of lots rejected by the establishment in a year divided by the number of lots attempted by the same establishment in the same year)
FDA Draft Guidance **July 2015**	= 1 – x (x = the number of specification-related rejected lots in a timeframe divided by the number of lots attempted by the same establishment in the same timeframe)
FDA Draft Guidance **November 2016**	= the number of accepted lots in a timeframe divided by the number of lots started by the same covered establishment in the current reporting timeframe

How these metrics have evolved

Product Complaint Rate

Russ Wesdyck, FDA **Dec 2013** (PDA Metrics Conference)	Not on original list
Brookings Quality Metrics Meeting, **May 2014**	Number of quality complaints / (Number of units released / 1 million)
Russ Wesdyck, FDA **Dec 2014** (PDA Metrics Conference)	= the number of complaints received by the manufacturer of the product concerning any actual or potential failure of an unit of drug product to meet any of its specifications, divided by the total number of lots released by the manufacturer of the product in the same year
FDA Draft Guidance **July 2015**	= the number of product quality complaints received for the product divided by the total number of lots of the product released in the same timeframe
FDA Draft Guidance **November 2016**	= the number of product quality complaints received for the product divided by the total number of dosage units distributed in the reporting timeframe

How these metrics have evolved

Invalidated OOS Rate

Russ Wesdyck, FDA **Dec 2013** (PDA Metrics Conference)	OOS / Laboratory Failure Investigation Rates
Brookings Quality Metrics Meeting, **May 2014**	**Confirmed** OOS Rate = Number of confirmed OOS / number of release tests conducted
Russ Wesdyck, FDA **Dec 2014** (PDA Metrics Conference)	**Invalidated** OOS Rate =the number of OOS test results invalidated by the establishment, or contracted establishment in a year divided by the total number of tests performed by the establishment in the same year
FDA Draft Guidance **July 2015**	**Invalidated** OOS Rate = the number of OOS test results for the finished product invalidated by the establishment divided by the total number of OOS test results divided by the total number of tests performed by the establishment in the same timeframe
FDA Draft Guidance **November 2016**	**Invalidated** OOS Rate = the number of OOS test results for lot release and long term stability testing invalidated by the covered establishment due to an aberration of the measurement process divided by the total number of lot release and long-term stability OOS in the current reporting timeframe

How these metrics have evolved

The 4th Metric

Russ Wesdyck, FDA **Dec 2013** (PDA Metrics Conference)	Only 3 Metrics
Brookings Quality Metrics Meeting, **May 2014**	Recall Rate
Russ Wesdyck, FDA **Dec 2014** (PDA Metrics Conference)	Right First Time
FDA Draft Guidance **July 2015**	APR / PQR on Time Rate (plus Optional Metrics)
FDA Draft Guidance **November 2016**	Only 3 Metrics

25 Required FDA Data Elements

14 are Master Data

	Element
1	Product Name
2	Rx/OTC
3	OTC Monograph
4	Product Type
5	Applicant Name
6	Application Type
7	Application Number
8	NDC Product Number Codes
9	Reporting Time Period
10	Quarter
11	Dose Form
12	Active Ingredient
13	Supply Chain/Process Stage Code
14	FEI/DUN

** Based on FDA 2016 Revised Guidance Appendix A.1*

25 Required FDA Data Elements

11 are Transactional Data

	**Line	Element
1	267	The number of saleable lots started which are intended for primary packaging or distribution
2	270	The number of saleable lots released for primary packaging or distribution
3	272	The number of saleable lots started which are intended for primary packaging or distribution and were rejected
4	275	The number of lots started of in-process and packaging product lots which are intended for distributed product
5	278	The number of in-process and packaging product lots released which are intended for distributed product
6	281	The number of in process and packaging product lots which were intended for distributed product and were rejected
7	307	The number of lot release test OOS and long term stability OOS results for the finished drug product or API where the long-term stability test supports the labeled expiration date
8	311	The total number of lot release and long-term stability tests conducted for the finished drug product or API where the long-term stability test supports the labeled expiration date
9	315	The number of OOS results for lot release tests and long term stability tests for the finished product or API where the source of the OOS result is identified as an aberration of the measurement process and where the stability test supports the labeled expiration date
10	363	The number of product quality complaints received for the product
11	365	The number of dosage units distributed for the product

*** Based on FDA 2016 Draft Guidance Line Number*

Learnings (So Far)…

- **Standardized Definitions:**
  - Inconsistent implementation and interpretation within a company (across sites).
  - Compounded when trying to standardize across a diverse industry.
- Current draft guidance metrics **do not mirror** common industry metrics.
  - **Value versus Effort**
- Further investment in IT systems required to deliver metrics as currently written.
  - Most systems designed to deliver **site** metrics
  - Not as easy to collect **product** metrics across its supply chain
- Industry engaged in the Quality Metrics discussion
  - …and open dialog with FDA

….Learnings (So Far)

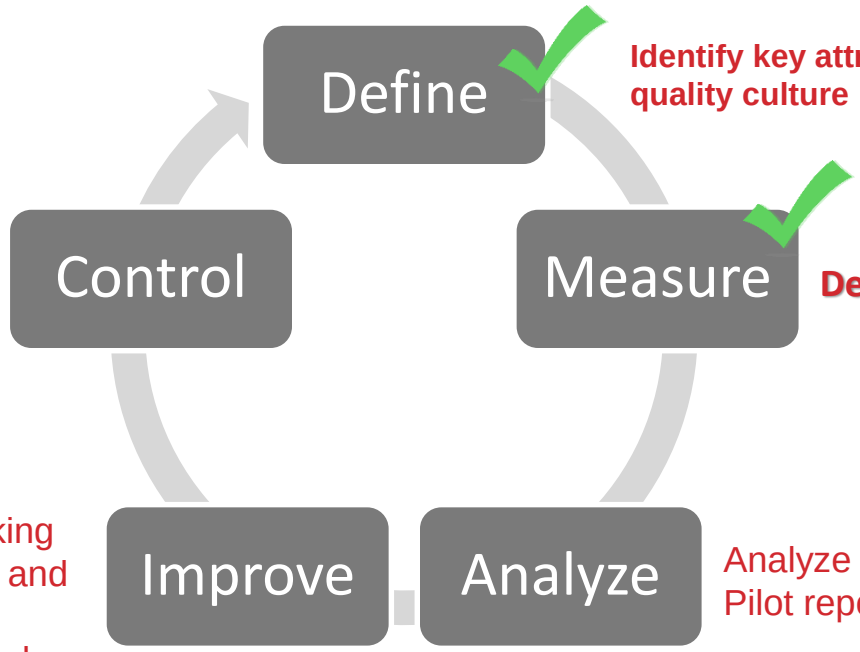
- Trending is most important
- Optimizing a metric program takes time to evolve
- Focusing on a metric can compromise its utility
- Finding forward looking metrics is very difficult
- Metrics has to be combined with a strong Quality Culture to be meaningful

PDA Quality Metrics Task Force

- **Steven Mendivil** (Chair)
- **Denyse Baker** (PDA)
- **Cylia Chen-Ooi** (Amgen)
- **Veronique Davoust** (Pfizer)
- **Marci Goldfinger** (J&J)
- **Shin-ichiro Mohri** (Kyowa Hakko Kirin Co)
- **Marty Nealey** (Hospira)
- **Pritesh Patel** (Novartis)
- **Edwin Rivera-Martinez** (Sanofi-Pasteur)
- **Anil Sawant** (Merck)
- **Siegfried Schmitt** (Parexel International)
- **Susan Schniepp** (Regulatory Compliance Associates)

Speaking of Quality Culture….

Where are we in the Quality Culture Journey?



Identify key attributes of quality culture

Develop & pilot the tools

Analyze key learnings
Pilot report – Q1 2018

- Continue benchmarking
- Discussion sessions and workshops to share improvement approaches

- Sustainability approaches

PDA Quality Culture Program

- Presented assessment of Pilot at PDA/FDA (Sep 2017)
- Initiated PDA Quality Culture Interest Group
- Enroll more participants in the PDA program to enhance understanding and drive improvement of quality culture
- Continue to build a robust benchmarking database and collect inputs from participants on improvement approaches
- Host upcoming workshops, conferences and publications to share key learnings from improving quality culture, do's and don'ts

Be Transformed!!

PDA's Culture Transformation Resources:

Course: Hands On Active Learning

Tool: Quantitative Assessment

Survey: Blinded, direct employee feedback

Benchmark: Compare against sites in Europe, North America, Asia

Join over 40 other sites who have already started their journey!

www.pda.org/transform

"This is the best PDA Course I have ever taken!"

–Stephan Krause, PDA Member

Be Transformed!!

What are most important positive quality culture behaviors that impact product quality?

Can you identify which mature quality attributes have the biggest impact on quality culture behavior?

Would you like to quantify the strengths and weaknesses of quality culture maturity at your plant site?

Take the first step on a journey to transform your Quality Culture with resources developed by PDA volunteers specifically for pharmaceutical manufacturing sites.

Following a successful pilot conducted over the last 18 months, PDA is pleased to launch the **Quality Culture Transformation Resources** to the industry.

When you enroll in this new program, PDA will train your assessors, teach you how to use the Maturity Model, offer an anonymous survey to your site staff and give you access to PDA's composite benchmarking results so you know where you stand with your peers.

Your site leadership will be able to gauge employees' views of quality culture and have a better understanding of where to take action, how to track progress, and which decisions to take to improve the site culture.

Course → Tool → Survey → Benchmark

PDA Quality Culture Transformation Resources

Your registration fee includes:

1. **COURSE** TWO seats in hands-on active learning in a two-day course on "Quality Culture Transformation"
2. **TOOL:** Quantitative assessment of current quality culture at TWO manufacturing sites
3. **SURVEY:** Blinded, direct employee feedback on aspects of your Quality Culture at TWO sites
4. **BENCHMARK:** Compare your results against more than 40 sites from 24 companies in North America, Europe, and Asia that have already completed Quality Culture Assessments.

Who Should Participate

This program will benefit pharmaceutical and biopharmaceutical manufacturing leaders who want to measure quality culture maturity at their plant sites and identify areas for improvement. It will also prepare your assessors to conduct site evaluations in a consistent and verifiable manner using the PDA Model and Tools.

PDA

PDA Quality Culture Transformation Resources

January 30-31, 2018
Thousand Oaks, CA

Four easy ways to register –
Click: www.pda.org/Transform
Fax: +1 (301) 986-1093 (U.S.A.)
Mail: PDA Global Headquarters
4350 East West Highway, Suite 600
Bethesda, MD 20814 U.S.A.
Call: +1 (301) 656-5900 ext. 115

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Course Enrollee Assessor #1 — PDA Membership Number

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Site A Name: | Location
Site B Name: | Location

Registration January 30-31

Course, Tool, Survey, Benchmarking	Member and Nonmember	Additional Options
	Before Oct. 1, 2017 ☐ $8,000	**Per Extra Attendee Enrolled** ☐ $4,000
	After Oct. 1, 2017 ☐ $9,500	**Per Extra Site Participating** ☐ $1,500

Payment Options *All cards are charged in U.S.$.*

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Total amount $
Account Number | Exp. Date
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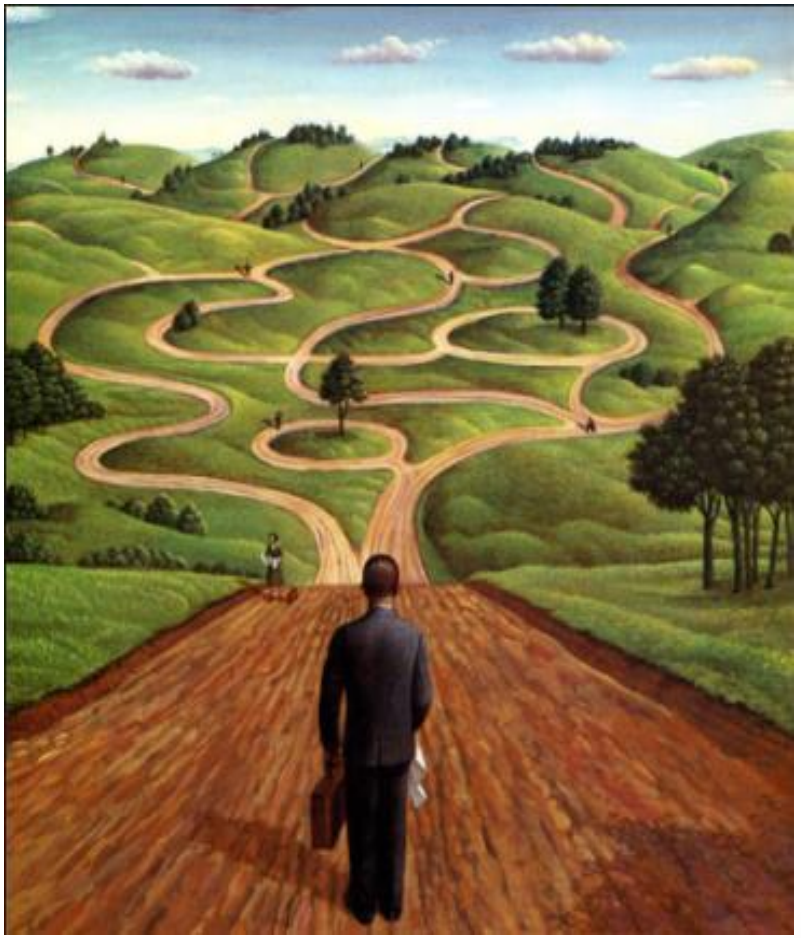
Gerald Heddell (MHRA)
PDA Staff: Denyse Baker, Rich Levy, David Talmage

Where are we now?

- Still a work in progress
- Ongoing dialogue
- Constructive feedback is important!
- *Paused* NOT stopped



Thank You!

Q & A