INTRODUCING ISPE

TIM HOWARD, PE CPIP
VICE CHAIR - ISPE BOARD OF DIRECTORS

SAAPI Conference
Bytes Conference Centre, Midrand
Friday, Oct 6th, 2017

Timothy P. Howard
Vice President
Commissioning Agents, Inc.

B.S. Mechanical Engineering

6 Years - Navy Nuclear Submarine Officer

20+ Years – Pharma / Biotech

18 Year member of ISPE

6 Years on ISPE International Board of Directors

Incoming Chair of ISPE Board

SME for QRM / Risk Based C&Q Topics

AGENDA

ISPE Purpose

Membership and Global Reach

Mission Statement / Strategic Plan

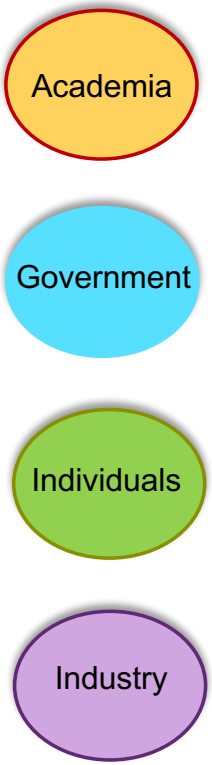
Body of Knowledge / Products and Services

Initiatives

ISPE Purpose Statement

ISPE delivers technical
and operational solutions to support our
Members across the global pharmaceutical
and biopharmaceutical industry in the
manufacture of quality medicines for patients

About ISPE



- Founded in 1980
- Not-for-profit, global professional society focused on bio-pharma tech & ops
- 18,000 individual Members from more than 90 countries
- Provides technological knowledge, education, and guidance documents for pharmaceutical industry
- Provides forums for exchange among industry, suppliers, academia, and regulators
- Strong ties with regulatory authorities worldwide

Who are Our Members?

Global pharmaceutical professionals from development through delivery:

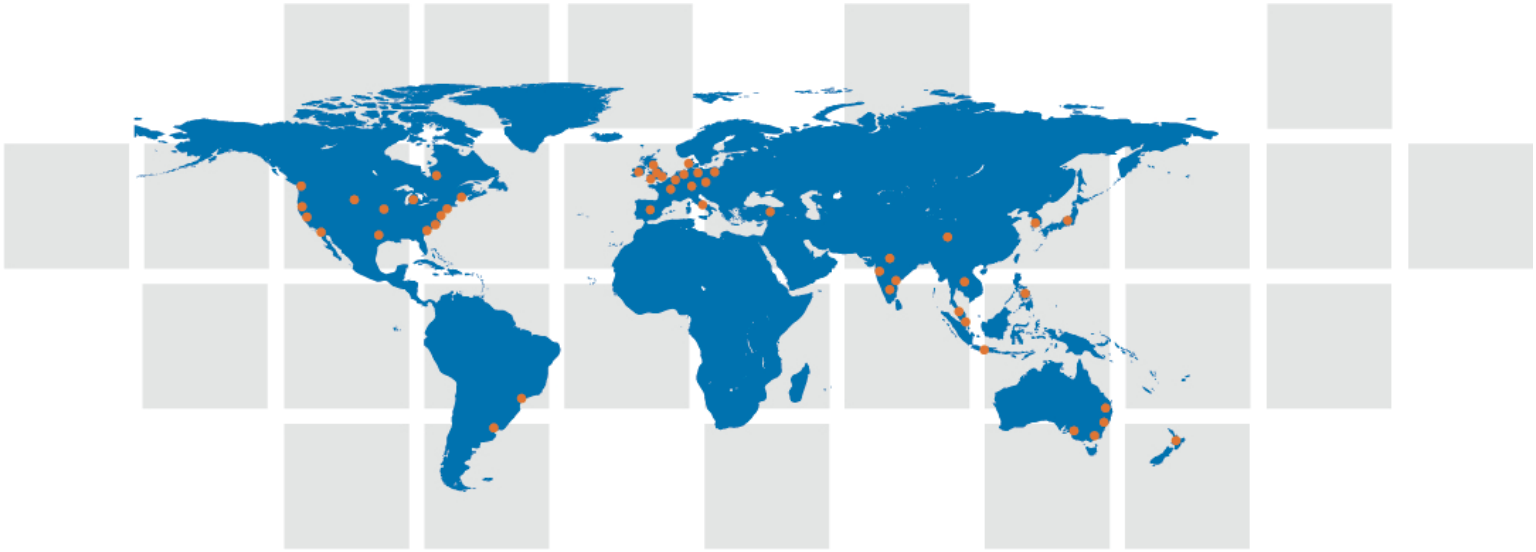
- Pharmaceutical Industry Professionals (biopharmaceuticals, APIs, generics, medical devices, and diagnostics)
- Contract Manufacturers
- Service/Equipment Suppliers
- Regulatory Authority Leaders
- Academics and Students

ISPE Global Presence

18,000+ Members

90 Countries

>40 Affiliates and Chapters



ISPE®

2016 - 2019 STRATEGIC PLAN


Biotechnology
Supply Chain
Quality and Performance
ISPE
Regulation
Facilities of the Future
Operational Excellence
Emerging Markets

Strategic Themes

RAPID INFORMATION DELIVERY

Ensure rapid and timely access to relevant technical resources anytime, anywhere

> Digital strategy and solutions for flows of information/content through multiple channels

> Rapid and lean process for content development and approval

> On-demand access to ISPE knowledge assets

Strategic Themes

DRIVING EFFICIENT MANUFACTURING OPERATIONS

Develop and share holistic industry business solutions to critical issues

- Emphasis on Biotechnology
- Business results-themed forums, guidance and training sharing deep insights derived from exchange with Members, companies, regulators, suppliers and other organizations
- Leadership in regulation associated to ISPE core concerns and priorities
- Foundational training and related knowledge exchange

Strategic Themes

LOCAL AND REGIONAL RELEVANCE

Understand and shape strategy to the business, culture and regulatory issues of local and regional markets

> Focus on a targeted emerging market initially; then work to develop next priority countries and/or regions

> Continue to deliver programs in Europe, US/North America and other regions relevant to the needs in the local markets

Strategic Themes

COMPELLING MEMBER AND INDUSTRY VALUE

Engage more individuals to join, learn and contribute

> Flexible regionally-pertinent ways for more individuals in the industry to engage with the organization

> Assets that are accessible, easy to understand, fit for purpose and capture user-generated feedback and knowledge

> Strong Membership brand equity

> Value perceived by companies and health authorities

Strategic Plan Summary Available for Download Here:

www.ispe.org/ispe-strategic-plan-summary

BODY OF KNOWLEDGE

PRODUCTS and SERVICES

Knowledge Network – Communities of Practice

Product Development & Production Systems Network

Active Pharmaceutical Ingredients

Biotechnology

Disposables

Oral Solid Dosage

PAT & Lifecycle Control Strategy

Product/ Process Development

Sterile Products Processing

Information Systems Network

GAMP®

Facilities and Equipment Network

Commissioning & Qualification

Containment

Critical Utilities

HVAC /Sustainable Facilities

Project Management

End to End Supply Chain Management Network

Investigational Products

Operations Management

Packaging

Guidance Documents – Baseline Guides

Volume 1 – API

Volume 2 – OSD

Volume 3 – Sterile

Volume 4 – Water and Steam Systems

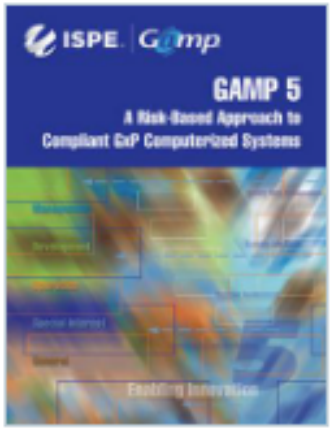
Volume 5 – C&Q

Volume 6 – Biopharm

Volume 7 – Risk Based Manufacture of Pharmaceutical Products (Risk-MAPP)

Guidance Documents

GAMP – Good Automation Manufacturing Practices



GAMP 5 Guide: Compliant GxP Computerized Systems

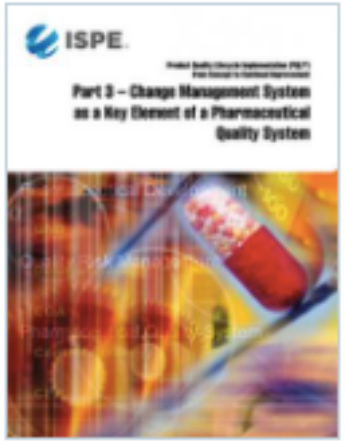
GAMP Guide: Records & Data Integrity

24 Good Practice Guides
2 Guides

Topics Include

- *Maintenance*
- *Process Gases*
- *Ozone Sanitization of Water systems*
- *Packaging and Labeling*
- *HVAC*
- *Good Engineering Practices*
- *Risk Based C&Q*

Product Quality Lifecycle Implementation



Product Quality Lifecycle Implementation Guide: Change Management System

Topics Include

- *Change Management*
- *Process Performance and Product Quality Monitoring System*
- *Product Realization*
- *Product Realization – Illustrative Example*

Conferences

2017 Asia Pacific GAMP Data Integrity Conference
13 November 2017 - 14 November 2017
Singapore

2017 Europe Pharma 4.0 Conference
23 November 2017 - 24 November 2017
Pescantina Verona, Italy

2017 Biopharmaceutical Leadership Forum
03 December 2017
San Francisco, CA USA

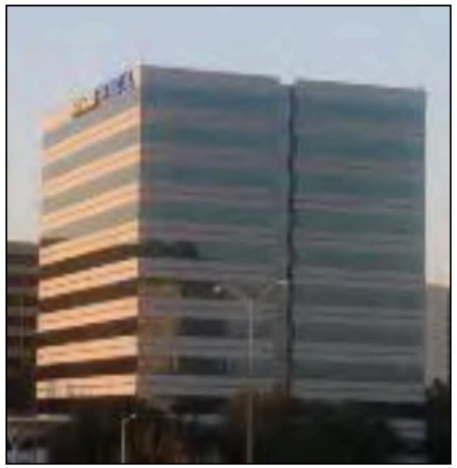
2017 Biopharmaceutical Manufacturing Conference
04 December 2017 - 06 December 2017
San Francisco, CA USA

2018 Aseptic Conference
06 March 2018 - 07 March 2018
Reston, VA USA

2018 Europe Annual Conference
19 March 2018 - 21 March 2018
Rome, Italy

2018 Quality Manufacturing Conference
04 June 2018 - 06 June 2018
Arlington, VA USA

Training Products



ISPE Training Institute and global training events

eLearning

Onsite

- North American Training Schedule

ISPE®

2017 ISPE Training Schedule

MARCH

ISPE Training Institute, Tampa, FL

- Bio Manufacturing Process Validation, 27 – 28 Mar.
- Technology Transfer, 16 – 17 Mar.

APRIL

ISPE Training Institute, Tampa, FL

- Bio Manufacturing Overview, 3 – 4 Apr.
- Oral Solid Dosage, 3 – 4 Apr. – ***Updated!***
- Q7A, 5 – 6 Apr. – ***Updated!***
- Cleaning Validation, 6 – 7 Apr.
- GAMP® 5, Annex II/Part II, 26 – 28 Apr. – ***Updated!***

MAY

ISPE Training Institute, Tampa, FL

- Clean-in-Place, 18 – 19 May – ***Updated!***
- Commissioning & Qualification, 18 – 19 May

San Diego, CA

- Bio Manufacturing Facilities, 8 – 9 May* – ***Updated!***
- GAMP® 5 Data Integrity, 8 – 9 May – ***Updated!***
- Water Generation, 8 – 9 May – ***Updated!***
- HVAC, 9 – 11 May – ***Updated!***
- Sterile Facilities, 10 – 11 May
- Water Storage, Delivery, and Qualification, 10 – 11 May – ***Updated!***

JUNE

ISPE Training Institute, Tampa, FL

- Quality by Design, 1 – 2 June
- GAMP® 5 Process Control Systems, 8 – 9 June – ***Updated!***
- Basic GAMP® 5, Annex 11/Part 11 Training Course, 12 – 14 Jun – ***Updated!***
- Pharma Water Generation USP WFI & PW Training Course, 12 – 13 Jun
- Storage/Qualification of Pharma Water Training Course, 14 – 15 Jun
- Water Generation, 12 – 13 June – ***Updated!***
- Water Storage, Qualification, 14 – 15 June – ***Updated!***

JULY

ISPE Training Institute, Tampa, FL

- HVAC, 10 – 12 July
- Oral Solid Dosage, 13 – 14 Apr. – ***Updated!***

AUG.

ISPE Training Institute, Tampa, FL

- Clean In Place, 7 – 8 Aug. – ***Updated!***

SEPTEMBER

ISPE Training Institute, Tampa, FL

- C&Q Risk Management, 7 – 8 Sept.
- Bio Manufacturing Facilities*, 8 – 9 Sept.
- GAMP® 5 Data Integrity, 11 – 13 Sept. – ***Updated!***
- Process Validation in Biotech Manufacturing, 14 – 15 Sept.
- Facility Project Management*, 18 – 19 Sept.
- Pharmaceutical Facilities Management, 18 – 19 Sept.
- Process Validation, 25 – 27 Sept.
- QRM, Sept. – ***Updated!***

- New ISPE Training Partnerships in Europe

Collaboration with NIBRT and St. Gallen

INITIATIVES

Drug Shortages
The Remaining Challenge

Slides courtesy of Francois SALLANS

Chair of ISPE Drug Shortage Taskforce

VP Quality and Compliance and Chief Quality Officer, Johnson & Johnson

Ensuring Supply

Historically

- Patients and customers rely on manufacturers to deliver quality medicines.
- Industry was measured in terms of “customer service.”

Today

- Industry is accountable regarding drug shortage prevention.
- The ability to prevent drug shortages has socio-economic consequences.
- Drug shortage prevention is becoming a GMP requirement.
- **In some countries, it is becoming a legal requirement.**

ISPE's Drug Shortages Initiative

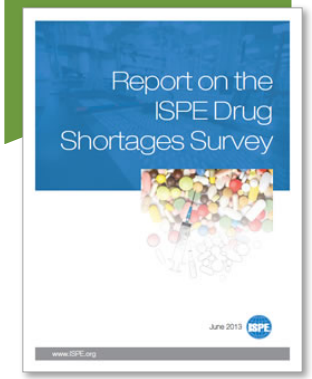
2012

- Drug Shortages
- Team formed

- Survey on root
- causes

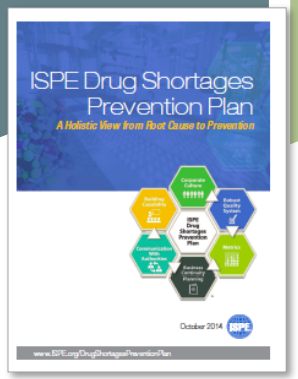
2013

- Survey learning
- shared with
- industry and
- regulators



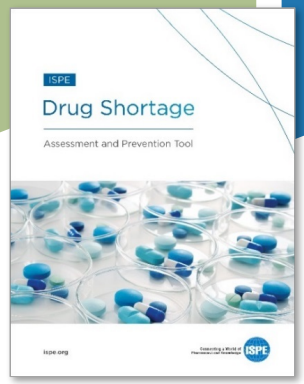
2014

- *ISPE Drug*
- *Shortages*
- *Prevention Plan*



2015

- *ISPE Drug Shortage*
- *Assessment and*
- *Prevention Tool*



2016

- ISPE Drug Shortages Webinar

- Drug Shortage
- prevention
- recognition added to FOYA program

2017

- Pew-ISPE Research Project on Drug Shortages

ISPE—Pew Initiative

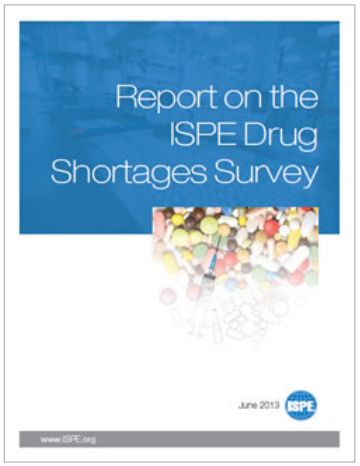
The Report explored market forces and companies' supply chain and business continuity investment decisions, and their relationships to drug shortages.

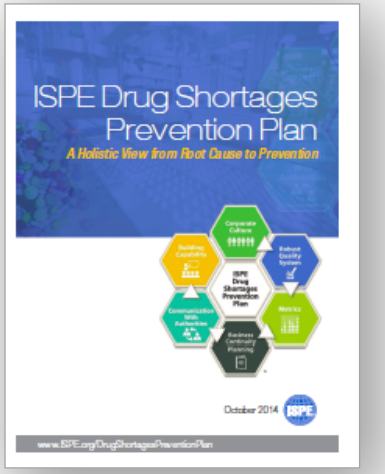
The Pew Charitable Trusts and ISPE, supported by PwC, conducted a unique, collaborative research project to:

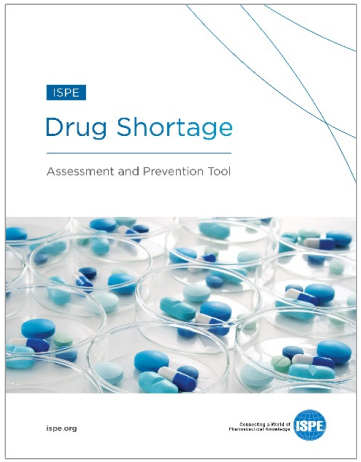
- Identify the multidimensional set of drivers behind shortages of sterile injectable drugs in the U.S.
- Find out whether the decisions companies made to reduce risks of future shortages were influenced by correlations between drug shortages and elements other than quality-focused factors

Download the
ISPE Drug Shortage Resources
at

www.ISPE.org/drug-shortages-initiative







Available freely to ISPE members and regulators.

ISPE Drug Shortages Introductory Webinar

Webinar Outline:

- Drug Shortages around the world – do we have a problem?
- What are the regulatory expectations regarding drug shortages?
- The ISPE drug shortages initiative: How did it start and what has it achieved.
    - Deeper review of
        - The Drug Shortages Survey results and identifying root causes.
        - The ISPE Drug Shortages Prevention Plan six dimensions
- Practical tools for use in preventing shortages

Current and Future Activities

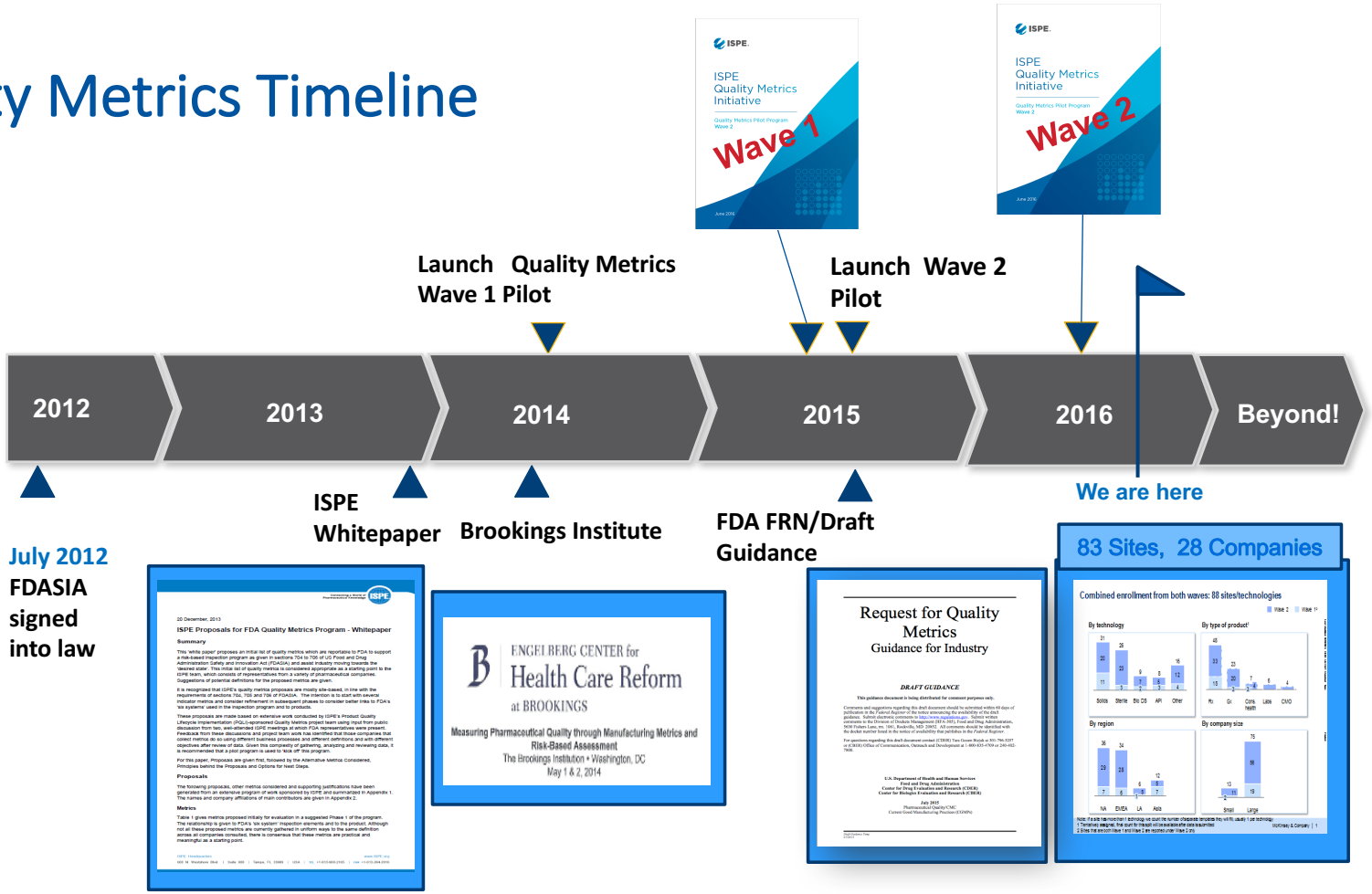
- **Collaborative research project with Pew Charitable Trusts**
  - Explores relationship between market forces, internal decisions, and shortages of sterile injectable products.
  - Scope: small, medium and large manufacturers of branded and generic sterile injectable products sold in the U.S.
  - Findings and insights to be released in Q4 2016.
  - Builds on ISPE's earlier drug shortages work.

- **Recognition of industry's prevention and preparedness**
  - Beginning in 2016, recognized as part of the ISPE Facility of the Year Awards program.

QUALITY METRICS INITIATIVE

Brief overview

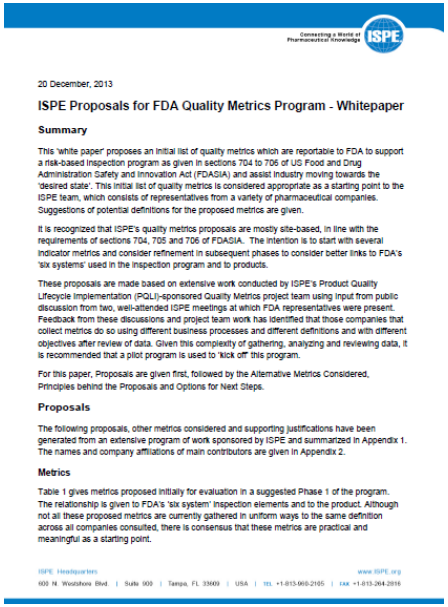
ISPE Quality Metrics Timeline



ISPE Proposals for FDA Quality Metrics

White Paper December 2013

- **Phased approach recommended**
- **Targeted set of metrics proposed**
- **Site Based reporting**
- **Pilot program**
  - Wave 1 then Wave 2



20 December, 2013

ISPE Proposals for FDA Quality Metrics Program - Whitepaper

Summary

This 'white paper' proposes an initial list of quality metrics which are reportable to FDA to support a risk-based inspection program as given in sections 704 to 706 of US Food and Drug Administration Safety and Innovation Act (FDASIA) and assist industry moving towards the 'desired state'. This initial list of quality metrics is considered appropriate as a starting point to the ISPE team, which consists of representatives from a variety of pharmaceutical companies. Suggestions of potential definitions for the proposed metrics are given.

It is recognized that ISPE's quality metrics proposals are mostly site-based, in line with the requirements of sections 704, 705 and 706 of FDASIA. The intention is to start with several indicator metrics and consider refinement in subsequent phases to consider better links to FDA's 'six systems' used in the inspection program and to products.

These proposals are made based on extensive work conducted by ISPE's Product Quality Lifecycle Implementation (PQLI)-sponsored Quality Metrics project team using input from public discussion from two, well-attended ISPE meetings at which FDA representatives were present. Feedback from these discussions and project team work has identified that those companies that collect metrics do so using different business processes and different definitions and with different objectives after review of data. Given this complexity of gathering, analyzing and reviewing data, it is recommended that a pilot program is used to 'kick off' this program.

For this paper, Proposals are given first, followed by the Alternative Metrics Considered, Principles behind the Proposals and Options for Next Steps.

Proposals

The following proposals, other metrics considered and supporting justifications have been generated from an extensive program of work sponsored by ISPE and summarized in Appendix 1. The names and company affiliations of main contributors are given in Appendix 2.

Metrics

Table 1 gives metrics proposed initially for evaluation in a suggested Phase 1 of the program. The relationship is given to FDA's 'six system' inspection elements and to the product. Although not all these proposed metrics are currently gathered in uniform ways to the same definition across all companies consulted, there is consensus that these metrics are practical and meaningful as a starting point.

ISPE Wave 1 Pilot – *What Did We Learn?*

Feasible to collect standardized set of metrics

Few companies aggregate metrics across supply chain to be able to report at product, differentiated by site

44 Sites, 18 Companies, 14 Metrics

Level of Burden not to be underestimated

Understanding data context is crucial

Start with a targeted set of "relatively well established" metrics

Gained early insights into quality culture that merit further exploration

Key benefits reported from Pilot Participants:

- ***Gaining a deeper understanding of the standardized metrics definitions and design***
- ***Establishing a centralized submissions process trial***
- ***Developing access to a benchmarking report that allowed them to examine progress against peers***

FDA Guidance Issued - *What Did We See?*

August 10 2016
FDA announced a revised draft to be issued before end of 2016

Key items

- **Covered Establishments & Reporting Establishments**
- **Included Metrics**
  - **4 Reportable Metrics**
    - 10 data collection points (4 X per year)
  - **Optional metrics**
    - Quality Culture & Process Capability
- **Data Reporting**
  - Product differentiated by site
- **Questions / dialogue encouraged**

Wave 2 Pilot Objectives

Initial

- **Expand the data set across segments, geographies and time to further the learnings from Wave 1 and evaluate trending patterns**
- **Continue to develop measures, tools and dialogue related to Quality Culture and Process Capability to facilitate on-going industry self-development and assessment**
- **Enable continued objective and data-driven dialogue with FDA and other Health Authorities.**

POST FDA GUIDANCE

- **Test the proposed FDA metrics**
  - Help develop appropriate definitions
  - Understand data collection challenges
- **Evaluate logistics and effort of gathering data at a product application level**

Key Findings from Wave 2

- Increase Participation and Interest
- Effort to collect metrics data 3X given in Federal Register Notice by FDA
- FDA Metrics showed relationship with Culture Indicators
- ISPE Comment to consider alternate definitions confirmed
- Quality Culture Important – But hard to measure
- For more detail – see Appendix and Wave 2 Report available from ISPE website

ISPE Proposals from Wave 2

Supports the recommendations given in response to the Guidance that ISPE:

- **Supports FDA's effort**
- **Start Small – Targeted Approach**
- **Phased Approach**
- **Recommends 3 metrics initially**
- **Some items deferred**
- **Burden to collect data is underestimated**
- **Transparency relative to data assessment as well as outcomes**

ISPE Quality Metrics - *Upcoming Key Activities*

- **Provide FDA Feedback**
- **Sharing ISPE Wave 2 Pilot outcomes with regulators globally**
- **Continue engagement in cross-industry dialogue**
- **Next Update**

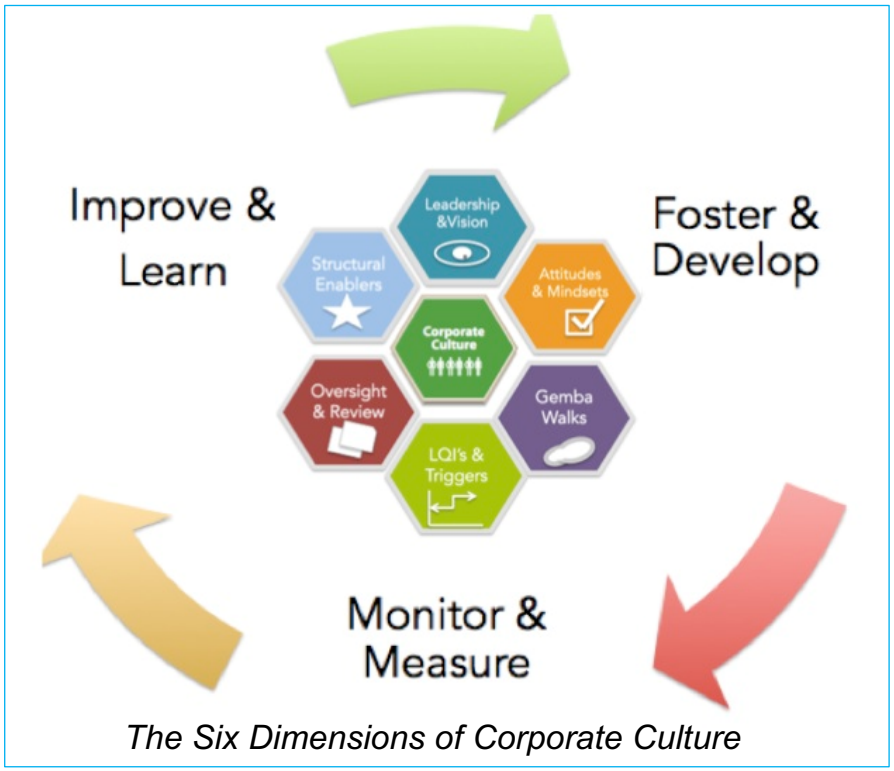
Quality Metrics Session
2016 ISPE Annual Meeting
Wednesday, 21 September
Atlanta, Georgia

Links:

- **For more information:**
  http://www.ispe.org/quality-metrics-initiative
- **Webinar and Reports from Pilot Wave 1 and 2:**
  http://www.ispe.org/quality-metrics-initiative/news
- **FDA Draft Guidance Request for Quality Metrics**
  http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm455957.pdf
- **ISPE Comments on FDA Draft Guidance**
  http://www.ispe.org/global-regulators/ispe-comments-regulations

ISPE's *Cultural Excellence Report* and Tools

- The work of ISPE's Quality Culture Team (a sub-team of ISPE's Quality Metric's Team)
- A holistic assessment of and practical support for those elements required to foster, develop, monitor, measure, learn and ultimately improve an organization's corporate culture:
  - **Leadership and Vision**
    - Cultural Excellence Assessment Tool
    - Leader 5V Model
  - **Mindsets and Attitudes**
    - Quality Mindset Shift Job Aid
  - **Gemba Walks/Engagement**
    - GEMBA Assessment Job Aid
  - **Measuring LQIs and Triggers**
    - Linking Culture, Attitudes, and Behavior: The LQI Model
  - **Oversight and Review**
    - Quality Culture Maturity Assessment
  - **Cultural Enablers**
    - Cultural Enablement Guide
    - Behavioral Accountability Matrix
    - Continuous Improvement Road Map



The Six Dimensions of Corporate Culture

Women in Pharma

Slides courtesy of Fran Zipp
President and CEO of Lachman Consultant Services

The Vision

ISPE "Women in Pharma" will provide women in the pharmaceutical industry a forum for connecting and collaborating on technical and career advancement topics. A community of WIP mentors, resources across all levels, and educational sessions will be an enabler for career success and work-life balance.

Focus

- Academic
  - Support the overall charter of the Women in Pharma Operational Committee by developing linkages and partnerships with universities in order to increase enrollment of female students and faculty members in ISPE. Collaborate with Chapters, Affiliates and Young Professionals in all geographical areas where ISPE has a presence in order to leverage their involvement with attracting and retaining women in academia as ISPE members.

- Collaborations
  - Support the overall charter of the Women in Pharma Operational Committee by collaborating with Chapters, Affiliates and young professionals. Target current ISPE members, member companies and active Chapter and Affiliates to raise awareness and make the target audience aware of local and national events.

- Educational & Contributions
  - To develop and establish
    - ✓ Ongoing educational presence at the Chapter, International, and ISPE Annual meetings.
    - ✓ Establish presence via sponsored luncheon, cocktail hours, or booths at ISPE National and International Events.
- Marketing
  - To develop strategic marketing campaigns and initiatives that drive our organization's progress towards gender parity, assist with the growth and education of our membership and sponsor programs to assist women in various role in the pharmaceutical industry.

FOYA 2017
Facility of the Year Awards

Category Winners

Equipment Innovation
Cook Pharmica
Location: Bloomington, Indiana, USA
Project: Flexible Filling Line (FFL)

Facility Integration
Bristol-Myers Squibb
Location: Devens, Massachusetts, USA
Project: Biologics Development Building/Clinical Manufacturing Building

Facility of the Future
Eli Lilly and Company
Location: Indianapolis, Indiana, USA and Carolina, Puerto Rico
Project: Continuous Direct Compression Manufacturing Kits 2 & 3

Project Execution
Jazz Pharmaceuticals Ireland Limited
Location: Althone, Ireland
Project: Project Rock

Process Innovation
Eli Lilly and Company
Location: Indianapolis, Indiana, USA and Carolina, Puerto Rico
Project: Continuous Direct Compression Manufacturing Kits 2 & 3

Operational Excellence
Abbott
Location: Longford, Ireland
Project: Operational Excellence – A New Quality Approach

Honorable Mentions

Nephron Pharmaceuticals Corporation
Location: West Columbia, South Carolina, USA
Project: Nephron SC

Novartis-Penn Center for Cellular Therapies
Location: Philadelphia, PA, USA
Project: Novartis-Penn Center for Cellular Therapies

PT Kalbio Global Medika
Location: Jakarta, Indonesia
Project: Biotech Facility

ISPE

2017 ANNUAL MEETING & EXPO

DRIVING INNOVATION TO ADVANCE PATIENT THERAPIES

29 Oct. – 1 Nov. | San Diego, CA

Meet the challenges of organizational and regulatory complexities to transform new medicines and technologies from vision into reality for patients around the world.

- **Technical Solutions**
- **Innovative Approaches**
- **Emerging Trends**
- **Targeted Technical Sessions**
- **In-Depth Workshops**
- **Career Enhancement Opportunities**

KEYNOTE SPEAKERS

Pam P. Cheng
Executive Vice President of Global Operations & IT
AstraZeneca

Roger Connor
President Global Manufacturing and Supply (GMS)
GlaxoSmithKline

Glenn F. Pierce, MD, PhD
World Federation of Hemophilia Board of Directors and Former Senior Vice President Hematology, Cell and Gene Therapy
Biogen, Inc.

Register Now! www.ISPE.org/2017-Annual-Meeting

Thank You!

Timothy P. Howard, CPIP, PE

ISPE Vice Chair – International Board