Attaining and Sustaining Quality
A Metris & Cultural Perspective

Fourth Pharmaceutical Science & QbD Conference
Hebrew University

Jerusalem
May 20, 2014
Louis W. Yu, Ph.D.
“A maximally efficient, agile, flexible pharmaceutical manufacturing sector that reliably produces high quality drugs without extensive regulatory oversight.”

Are we there yet?
Customer Centric Quality & Procedural Compliance Quality

• Quality is meeting customer requirements

• Consumers want drug products to be:
  – Effective when used as directed
  – Safe as labelled
  – Available when needed
  – Affordable

• Pharmaceutical Industry
  – have achieved a high level of quality as viewed from consumers perspectives (SISPQ)
  – Opportunities for continuous improvement to deliver consistently high standard of quality when viewed in the context of procedural compliance as indicated by trends in FARs, 483 observations, class 2 & 3 recalls & drug shortages of certain drugs
FDA/CDER’s Evolving Approach to Quality and the Use of Metrics

Russell Wesdyk
CDER/OSP
March 14, 2014
FDA Restructuring CDER to form OPQ

Office of Pharmaceutical Quality

Sub Office Roles

• Product Review – “What the product is and how designed”
  – Define effective clinically relevant product specifications... create standards that matter for patients

• Process/Facility Review – “How and where its made”
  – Focus on process... conduct high risk PAIs, an integrated model

• Surveillance – “How products and firms perform over lifecycle”
  – Assess and make quality visible and impactful
ONE OF OPQ 8 SUB-OFFICES

OFFICE OF SURVEILLANCE & QUALITY METRICS
Concur with FDA Articulated Consensus Goals

- For firms, the use of quality metrics promotes responsible practices and quality driven corporate culture
- For public, a focus on quality leads to fewer recalls and quality related shortages
- For FDA, industry achieves and is rewarded for quality, without extensive regulatory oversight
Us of Metrics to:
Ensure customers receive acceptable product
Track organization performance
Advance continuous improvement quality culture

“Focus of attention is the message”
We welcome FDA focus on metrics

“Behavior is a function of Consequences”
We hope Regulators avoid unintended consequences in this initiative
Quality Metrics

- How many is too many?
- Are these the right indicators?
- Are they driving the desired outcome?
- How are they helping us in the area of sustainability?
- Do they provide a holistic picture of quality and compliance?
The Correct Metrics, Not More Metrics

Law of diminishing returns – after a while, too many numbers become overkill
Extensive Industry Engagement by FDA (White Papers and Conferences)

- BIO
- CHPA
- GPHA
- ISPE
- PDA
- PHRMA
- Individual Companies
- Brookings Institute Metrics Expert Workshop
ISPE/PDA/CHPA/Brookings Workshop provides Stakeholder Consensus Metrics

- Lot acceptance rate
- Product quality complaint rate
- Confirmed OOS rate
- Recall rate
Office of Surveillance Implementation of Q Metrics:

- Support FDA on evolving quality
- Shift focus from procedural compliance quality to customer centric quality - clinical relevant requirements & risk management
- Continue to focus on alignment of ORA & CDER approach to review, approval, surveillance, inspection, enforcement actions around QbD (process knowledge, effective control strategy, CpK), Quality risk management, Quality Systems effectiveness
- Continue to assure no unintended consequence when implementing global, pan industry Q metrics
- Concur with message on OTC/Rx sector differences and context
- Evolving adoption of Q metrics should be effective in moving the needle while avoiding unintended consequences
Albert Einstein:

“Not everything that can be counted count, and, Not everything that counts can be counted”
Perrigo Company
Legacy of Culture-Driven Success
HOW WE DEFINE QUALITY

QUALITY = E²C

EFFECTIVENESS  Consistently meeting customer requirements with products that are available when needed, at an affordable cost, that conform to requirements for Strength, Identity, Safety, Purity and Quality (SISPQ).

EFFICIENCY  Optimize resources needed to meet requirements using right first time execution and robust, lean processes.

COMPLIANCE  Continuously improving our systems and processes to dependably meet clearly-defined quality standards and regulatory requirements.
Sustaining Quality & Business Success - Culture Matters

127-year legacy of focusing on people – employees, customers, consumers and neighbors
Core Values & Five Pillars Remain the Foundation for Our Strategies

MISSION: QUALITY AFFORDABLE HEALTHCARE PRODUCTS™

CODE OF CONDUCT / CORE VALUES

QUALITY  CUSTOMER  INNOVATION  COST EFFECTIVENESS  PEOPLE

STRATEGY
One of the World’s Leading Healthcare Products Manufacturers with a Diverse Product Line

<table>
<thead>
<tr>
<th>Facilities</th>
<th>Solid Dose (Rx, OTC)</th>
<th>Liquids (Rx, OTC)</th>
<th>Semi-Solids (Rx, OTC)</th>
<th>Infant Formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>North America</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14 Plants</td>
<td>42 Billion Tablets</td>
<td>2.3 Billion Doses</td>
<td>800 Million Doses</td>
<td>36 Million Units</td>
</tr>
<tr>
<td>EU</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 Plants</td>
<td>4 Billion Tablets</td>
<td>50 Million Doses</td>
<td>400 Million Doses</td>
<td></td>
</tr>
<tr>
<td>Middle/Far East</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 Plants</td>
<td>1 Billion Tablets</td>
<td>500 Million Doses</td>
<td>100 Million Doses</td>
<td></td>
</tr>
<tr>
<td>Total:</td>
<td>47 Billion Tablets</td>
<td>2.8 Billion Doses</td>
<td>1.3 Billion Doses</td>
<td>36 Million Units</td>
</tr>
</tbody>
</table>

- 23 Total Sites
- 12 OUS Sites
- Over $3.5 Billion in Sales
- 9500+ employees
- Markets over 3000 products/18000 SKUs
IN 2014

every second of every day, somewhere in the world, 1,500 people will utilize a Perrigo product.
Customer Centric Quality

• Quality is meeting customer requirements
• Consumers want drug products to be:
  – Effective when used as directed
  – Safe as labelled
  – Available when needed
  – Affordable
• As a company
  – we have achieved a high level of quality as viewed from consumers perspectives (SIS PQ)
  – Some opportunities for continuous improvement when viewed in the context of procedural compliance
Finding a Path to Quality Sustainability

- Setting the course-Aligning Quality and Business Strategy
- Surveillance- Leading and Lagging indicators and transforming data into information
- Governance- Transforming information into knowledge and having the courage to act
Scale & Diversity of Products Impacts Metrics Collection

**Periodic Review**

- Applicable to all business units?
- Predictive of future performance?
- Clear Definitions and Calculations?
- Drives culture and ‘moves the needle’?
- Trend-Based or Point-Based evaluation?

**Product Quality Metrics**
- Assess Product Quality
- Verify a State of Control

**Site Quality Metrics**
- Assess site processes
- Verify a State of Control
Assuring Patient Safety - End to End Supply Chain Security & Integrity

Internal Support Services & Quality, EHS, Engineering, IT, Facilities

Supplied Materials/Products → Products/Service Design & Development → Manufacturing & Testing → Packaging → Warehouse & Distribution → End User / Customer

External Contracted Services
Manufacturing, Testing, Artwork & Origination, Packaging, Warehousing & Distribution, Calibration
Sustainable Quality Vision Drive Strategies

- **Quality Risk Management**
  - Product & customer safety as highest priority
  - Manage constantly evolving quality and compliance expectations

- **Process Excellence**
  - Meet quality and compliance expectations balancing cost & risk/benefit to remain competitive
  - A continuous improvement culture

- **Built in Product Quality**
  - Full product life cycle quality-by-design
  - Quality into supply chain

- **Innovation & Growth**
  - Speed to market, flexibility and competitiveness without sacrificing consistent product quality and compliance
  - Incorporate a global, integrated manufacturing and supply chain to complying with regulatory and corporate standards

- **Human Capital Enhancement**
  - A scalable organizational structure to support product lifecycle and organic/inorganic global growth
  - Processes and mechanisms to develop a learning organization
Aligning Quality and Business Strategy - Robust Quality Capability & Culture

**The Quality Plan**

- **Management Controls**
  - Mgmt. Oversight & Support
  - Quality Oversight
  - Staffing

- **Human & Organizational Performance**
  - SOP Compliance
  - Training
  - Quality Culture
  - Performance Management

- **Quality System**
  - Packaging & Labeling
  - Cleaning
  - Deviation Process
  - Production Control improvements

- **Business Operational Strategy**
  - Operational Simplification
  - Organization
  - Facilities, Equipment & Technology Investments

Improve GMP Control through Prevention, Detection & Correction
Perrigo EEC Quality Metrics

Effectiveness

- CAPA Past Due
  - Leading
- Human Error Reduction
  - Leading
- Confirmed Customer Complaints
  - Lagging

Efficiency

- Total Cost of Quality
  - Leading
- Right First Time
  - Leading
- Monetary Amount on Quality Hold
  - Lagging
- Field Alerts/ Equivalent Regulatory Reporting
  - Lagging

Compliance

- Regulatory Compliance Status
  - Lagging
- Recalls/Withdrawals
  - Lagging
## Supporting Metrics Gathered

<table>
<thead>
<tr>
<th>Metric</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Deviations Generated</td>
</tr>
<tr>
<td>Total Deviations Pending</td>
</tr>
<tr>
<td>Deviations Open Past 60 Days</td>
</tr>
<tr>
<td>Open Pending CAPAs</td>
</tr>
<tr>
<td>Lab RFT</td>
</tr>
<tr>
<td>Lab OOS Investigations</td>
</tr>
<tr>
<td>QC Staffing</td>
</tr>
<tr>
<td>QA Staffing</td>
</tr>
<tr>
<td>Production FG Units</td>
</tr>
<tr>
<td>Number of Manufacturing Batches</td>
</tr>
</tbody>
</table>
To attain & sustain quality, focus on organization capability & the one true leading indicator – Culture

**Quality Maturity**
- Effectiveness of CAPA
- Right 2nd Time
- Repeat Deviations

**Operational Excellence**
- Total cost of quality
- Quality Hold
- Right First time
- % Back order

**Organizational Readiness**
- Capital Investment in quality and compliance
- % of time per employee spent on learning
The Model for Shaping an Organizational Culture

- **Principles**: Guide the purpose of your:
  - **Systems**: Which encourage, reinforce, and drive:
    - **Behavior**: Which is your:
      - **Culture**
Culture is beliefs, Values & Behavior

<table>
<thead>
<tr>
<th>Principles</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Create Value for the Customer</td>
</tr>
<tr>
<td>2) Create Constancy of Purpose</td>
</tr>
<tr>
<td>3) Think Systemically</td>
</tr>
<tr>
<td>4) Focus on Process</td>
</tr>
<tr>
<td>5) Seek Perfection</td>
</tr>
<tr>
<td>6) Embrace Scientific Thinking</td>
</tr>
<tr>
<td>7) Flow and Pull Value</td>
</tr>
<tr>
<td>8) Assure Quality at the Source</td>
</tr>
<tr>
<td>9) Lead with Humility</td>
</tr>
<tr>
<td>10) Respect Every Individual</td>
</tr>
</tbody>
</table>

- Core Values (Respect, Responsibility, Integrity)
- 5 Pillars
- E²C Quality
- Quality Affordable Health Care
- Organizational Health

Slide courtesy of the Institute for Enterprise Excellence
Org. Health is the ability of an organization to align, enable, and improve itself faster than the competition to sustain exceptional performance over time. It is derived from the deeper understanding and focus of universal principles such as lead with humility, respect, and think systemically – aspects that traditional metrics don’t capture.
As Quality Culture of the organization matures, focus on KBIs

The focus will shift from pure performance to behaviors.
## KBI’s – Key Behavioral Indicators

Behaviors are describable, observable, recordable, How to quantify?

<table>
<thead>
<tr>
<th>Behavior</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>EC Members report at QBR their sites/functions progress to CI Action Plan.</td>
<td></td>
</tr>
<tr>
<td>Site leaders ensure accurate measurement, quantification, and reporting to</td>
<td>using Finance developed process</td>
</tr>
<tr>
<td>EC Members (using Finance developed process)</td>
<td></td>
</tr>
<tr>
<td>At assessments, EC member and site leadership complete 5 day workshop</td>
<td></td>
</tr>
<tr>
<td>Site leadership establish/maintain a resource plan to catalyze the program</td>
<td>from within</td>
</tr>
<tr>
<td>Site leaders show evidence of systems documentation/improvement post</td>
<td>assessment or after Build training</td>
</tr>
<tr>
<td>Managers coach/mentor scientific thinking</td>
<td></td>
</tr>
<tr>
<td>Leaders recognize the successes of their teams in building a Continuous</td>
<td>Improvement Culture ($, Quality, Teamwork, Customer Service)</td>
</tr>
<tr>
<td>Site balanced scorecards established for assessed sites (based on 5-pillars;</td>
<td>includes performance and behavior)</td>
</tr>
<tr>
<td>EC/Top Management Process Owners provide adequate resources for Process</td>
<td></td>
</tr>
<tr>
<td>Improvement success</td>
<td></td>
</tr>
</tbody>
</table>
Current Thought Leaders on Organization Effectiveness:
Culture trumps strategy – healthy trumps smart

• Smart/Value Focus
  – Quality
  – Growth
  – Leadership
  – Service
  – Strategy
  – Technology
  – Finance

• Healthy/Joy Focus
  – Truth
  – Honor
  – Beauty
  – Love
  – Justice
  – Minimum Politics
  – High Productivity
  – Low Turnover
Building A Health Organization
The 4 Principles
“The Advantage”

- Build a highly cohesive team
- Create Clarity
- Reinforce Clarity
- Over-communicate clarity
Building a highly cohesive team  
From Lencioni “The Advantage”

• Behaviors that foster vulnerable trust
• Effective use of conflicts
• Engender commitment
• Hold each team member and self accountable
• Generate sustainable results
Align on answers to the following:

1. Why do we exist?
2. How do we behave?
3. What do we do?
4. How will we succeed?
5. What is important now?
6. Who must do what?
Perrigo’s Healthy & Smart Culture

- Quality-driven – Right First Time
- Innovation through diversity of culture, thought, experience
- Culture of compliance – we do what’s right
- Focus on skills development and process excellence
- Open communication through various channels
Perrigo’s Core Values

**Respect**
*We demonstrate the value we hold for one another*

**Integrity**
*We do what is right*

**Responsibility**
*We hold ourselves accountable for our actions*
Perrigo’s Code of Conduct: We Are Responsible for…

• Complying with the law, policies and procedures
• Building trusting relationships with our customers, consumers and suppliers
• Dealing fairly with others
• Protecting our shareholders’ assets
• Avoiding conflicts of interest
• Fostering a positive work environment
• Conducting business with respect for local conditions
• Supporting our communities and the public
Survey Metrics Show Consistently Strong Employee Engagement

- **Consistently strong engagement levels from survey to survey**
  - Employees across Perrigo express strong commitment and effort levels, and would gladly recommend the company as a great place to work.
  - Retention levels exceed benchmark comparisons, and approach high performing company comparisons.
Engagement Strengths

- Belief in Perrigo's vision
- Commitment to Quality
- Understanding / commitment to Perrigo's goals & objectives
- Support for employee healthy / safety
- Belief that Perrigo has the right strategies in place to achieve vision
High Engagement Compared to Global Pharma

• Employees have confidence in Perrigo’s senior leadership.
  – Employees believe that Perrigo’s executives and business leaders set a good example of ethical business behavior.
  – Employees feel department/business unit leadership demonstrate that customer satisfaction is a top priority.

• Employees believe strongly in Perrigo’s vision, demonstrating strong commitment to quality and customers
  – Employees understand Perrigo’s goals and objectives, and believe in the company’s vision and commitment to quality.
  – Employees feel Perrigo provides them a healthy and safe place to work.

• Employees find their work to be interesting and stimulating
  – Employees feel their career goals can be met at Perrigo.
High Engagement Compared to Global Pharma (cont.)

• Employees believe that quality and customer service are key strengths, staying consistent with Perrigo’s core values.
  – Employees feel that day-to-day business decisions demonstrate that quality is a top priority
  – Employees feel an attitude of customer service permeates the company.
• Employees feel Perrigo has a culture that values their input
  – Employees feel encouraged to find new and better ways to do their work and that ideas are adopted regardless of who suggests them.
  – Employees consistently believe their department or business unit is committed to process improvement.
• Employees adapt well to change, and expect transparency and communication from their managers and site leadership teams.
  – Employees want to contribute to improvements and are generally willing to put in extra effort.
When it comes to sustainability - Culture matters: Strong, Consistent Revenue Growth FY 2008-2013

*See Appendix for reconciliation of adjusted operating margin to GAAP

Note: Organic sales exclude the effects of acquisitions; acquisitions and their subsequent growth remain in inorganic sales in years following the acquisition
Thank You

Questions?