Quality as Foundation for OPEX

Prof. Dr. Thomas Friedli

2nd FDA/PQRI Conference on Advancing Product Quality
Bethesda, October 6th, 2015
Structure

1. Introduction
2. Quality Management / FDA Quality Metrics Initiative
3. Operational Excellence and Quality
4. The Impact of Process Capability on Quality
5. Summary and Outlook
10 Hot Topics in Pharma from an OPEX Perspective

- Quality Metrics
- Benchmarking the Quality Org.
- Organizing OPEX
- OPEX Maturity
- Managing Complexity

- OPEX in Network
- Knowledge Management

OM: Operations Management; CI: Continuous Improvement
Costs in Pharmaceutical Development

<table>
<thead>
<tr>
<th>Company</th>
<th>Total R&amp;D Spending 1997-2011 (US$Mil)</th>
<th>Number of drugs approved</th>
<th>R&amp;D Spending Per Drug (US$Mil)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AstraZeneca</td>
<td>58,955</td>
<td>5</td>
<td>11,791</td>
</tr>
<tr>
<td>GlaxoSmithKline</td>
<td>81,708</td>
<td>10</td>
<td>8,171</td>
</tr>
<tr>
<td>Sanofi</td>
<td>63,274</td>
<td>8</td>
<td>7,909</td>
</tr>
<tr>
<td>Roche Holding AG</td>
<td>85,841</td>
<td>11</td>
<td>7,804</td>
</tr>
<tr>
<td>Pfizer Inc.</td>
<td>108,178</td>
<td>14</td>
<td>7,727</td>
</tr>
<tr>
<td>Johnson &amp; Johnson</td>
<td>88,285</td>
<td>15</td>
<td>5,886</td>
</tr>
<tr>
<td>Eli Lilly &amp; Co.</td>
<td>50,347</td>
<td>11</td>
<td>4,577</td>
</tr>
<tr>
<td>Abbott Laboratories</td>
<td>35,970</td>
<td>8</td>
<td>4,496</td>
</tr>
<tr>
<td>Merck &amp; Co Inc</td>
<td>67,360</td>
<td>16</td>
<td>4,210</td>
</tr>
<tr>
<td>Bristol-Myers Squibb Co.</td>
<td>45,675</td>
<td>11</td>
<td>4,152</td>
</tr>
<tr>
<td>Novartis AG</td>
<td>83,646</td>
<td>21</td>
<td>3,983</td>
</tr>
<tr>
<td>Amgen Inc.</td>
<td>33,229</td>
<td>9</td>
<td>3,692</td>
</tr>
</tbody>
</table>

Table of Research Spending per New Drug 1997-2011
(Source: The Truly Staggering Cost of Inventing New Drugs, Herper (2012))
Today’s Challenges in Operations Management

*Driver 2: Quality and/or delivery issues*

Today’s Challenges in Operations Management

Driver 3: Globalization
A Definition of Operational Excellence

The St.Gallen understanding

The ITEM-HSG defines Operational Excellence as a philosophy directing an organization towards continuous improvement!

- It is the balanced management of cost, quality and time focusing on the needs of the customer
- It comprises structural & behavioural changes to support the needed activities the best way possible
- To be sustainable it has to be pushed by Top Management and to be designed to engage every single employee

Operational Excellence is not only about performance, it is also about the way an organization achieves superior performance and about how it continuously improves itself!

Source: Friedli et.al. (2013), Leading Pharmaceutical Operational Excellence
The St. Gallen OPEX and the “Sand Cone Model”

Source: Friedli et.al. (2013), Leading Pharmaceutical Operational Excellence

Source: Ferdows/DeMeyer (1990), Journal of Operations Managementt
The St. Gallen Pharma OPEX Database

<table>
<thead>
<tr>
<th>Industry</th>
<th>Pharmaceutical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Production Sites</td>
<td>299 (Total)</td>
</tr>
<tr>
<td>▪ 217 (Formulation &amp; Packaging)</td>
<td></td>
</tr>
<tr>
<td>▪ 58 (API)</td>
<td></td>
</tr>
<tr>
<td>▪ 24 (Biotech)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Number of Companies</th>
<th>124 (Total)</th>
</tr>
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<tbody>
<tr>
<td>including eleven companies of the Top 20*</td>
<td></td>
</tr>
</tbody>
</table>

| Content – Scope           | Enabler Implementation and Performance Metrics (KPIs) |

<table>
<thead>
<tr>
<th>Content – Modules</th>
<th>Total Productive Maintenance (TPM)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total Quality Management (TQM)</td>
</tr>
<tr>
<td></td>
<td>Just-In-Time (JIT)</td>
</tr>
<tr>
<td></td>
<td>Effective Management System (EMS)</td>
</tr>
</tbody>
</table>


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1. Introduction
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The History of Quality Management

<table>
<thead>
<tr>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Antiquity</td>
<td>&quot;Guilds&quot;</td>
<td>Taylorism, management</td>
<td>Shewhart et al.</td>
<td>Quality assurance</td>
<td>• Integrated quality assurance, company-wide quality control, quality circles</td>
<td>System norms (ISO), TQM (awards)</td>
<td>Awards, IQM</td>
<td>Integrated, sustainable management</td>
</tr>
<tr>
<td>Egypt, pyramids, measurement</td>
<td>Norms, masters, companions</td>
<td>Work sharing, quality control</td>
<td>Random test plans</td>
<td>Precaution, defect avoidance in production</td>
<td>Other areas (R&amp;D, Sales) improvements</td>
<td>Quality management, general management</td>
<td>Top management integration, integration in management</td>
<td>Global reach, integration in society and environment</td>
</tr>
</tbody>
</table>

- **Technically oriented perspective**
- **Customer- & Stakeholder oriented perspective**

**ISO 9000 (2008):**

*Quality of a unit is the "degree to which a set of inherent characteristics fulfils requirements".*

**Short form:**

*Quality are the properties as measured against needs and expectations.*

Source: Seghezzi (2003)
Quality and Manufacturing today

“The independence of quality control from production is considered fundamental.” – WHO GMP for Pharmaceutical Preparations*

**Situation in Pharma Plant:** both department rather work against each other than cooperating in order to attain their individual targets and KPIs

“Without manufacturing there is no quality to control or assure” statement of a manufacturing department representative

“On-time-delivery and other manufacturing KPIs are not my business” statement of a quality representative

*Source: “WHO Expert Committee on Specifications for Pharmaceutical Preparations” Section 17.2. WHO technical report series; 908, 2001: Geneva, Switzerland

**Source: Project Example from 2015
Do we measure the right things?

<table>
<thead>
<tr>
<th>Airline Operations</th>
<th>Room Cleaning Operations</th>
<th>Production</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typical Metrics</td>
<td>On-Time departure</td>
<td>Minutes/m2</td>
</tr>
</tbody>
</table>

Source: Institute of Technology Management (ITEM-HSG), University of St.Gallen
Questions to ask!

 Do you measure and manage the system including business or single dimensions?

 Has your metrics been designed as sum of all KPI’s used somewhere anyway or was there a guiding logic?

 Do you take into account both main dimensions?:
  - «doing the right things» = efficacy / added value
  - «doing the things right» = efficiency

Source: Institute of Technology Management (ITEM-HSG), University of St.Gallen
FDA Draft Guideline – Suggested Metrics

- Lot Acceptance Rate
- Product Quality Complaint Rate
- Invalidated OOS Rate
- APR or PQR on Time Rate

Source: Draft Guidance “Request for Quality Metrics” from July 2015
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Quality as basis for OPEX

Quality Management System is based on OPEX and structured along different levers

Source: Institute of Technology Management (ITEM-HSG), University of St.Gallen
Quality Effectiveness

Supplier Reliability:
- Service Level Supplier
- Complaint Rate Supplier

Production Stability:
- OEE
- Unplanned Maintenance
- Right First Time
- Rejected Batches
- Scrap Rate
- Deviations per batch
- Deviation closure time

Delivery Quality:
- Forecast Accuracy
- Production Schedule Accuracy
- Service Level Delivery

Customer Quality:
- Complaint rate customer

Operational Excellence

Quality Management System

Quality Effectiveness
Management System Performance
Quality Enabler

Your site
Industry average
Quality Efficiency

- Quality Costs/Overall Costs
- FTE Quality Control/Total FTE
- FTE Quality Assurance/Total FTE

- Maintenance Costs/Overall Costs
- Cost Preventive Maintenance
Management System Performance

EMS:

- Quantity of Suggestions
- Quality of Suggestions
- Sick Leave
- Training Days
- Level of Qualification
- Level of Safety
- Employee Turnover
Quality Enabler

Preventive:
- Preventive Maintenance
- Housekeeping
- Process Management
- Cross functional development
- Supplier Quality Management
- Visual Management
- Planning adherence
- Functional Integration

Management Commitment:
- Management Commitment & Company Culture

Continuous Improvement:
- Customer involvement
- Employee involvement and CI
- Standardization and simplification
OPEX and Quality

A high OPEX performance indicates a high overall Quality system performance.
OPEX and Quality

OPEX high performers have a high Quality Effectiveness, Efficiency and a very good Quality Culture

Source: Institute of Technology Management (ITEM-HSG), University of St.Gallen
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The Impact of Process Capability on Quality & Excellence

TPM
Performance:
- OEE
- Setup & Cleaning
- Unplanned Maintenance

Enabler:
- Preventive Maintenance
- Housekeeping

TQM
Performance:
- Complaint Rate Customer
- Deviation Closure Time
- Deviations per Batch
- Quality Cost/Overall Cost
- Rejected Batches
- Scrap Rate
- Yield
- RFT

Enabler:
- Cross Functional Product Development
- Customer Involvement
- Planning Adherence

JIT
Performance:
- Forecast accuracy
- Service Level Delivery
- Total time for changeover
- Production Lead Time
- Order Lead Time
- Finished Good Turns
- WIP Turns
- Raw Material Turns
- Production schedule...
- Replacement time

Enabler:
- Setup time Reduction
- Pull Production
- Layout Optimization

Legend:
- High Performer
- Low Performer
The Impact of Process Capability on Quality & Excellence

<table>
<thead>
<tr>
<th>Process Management</th>
<th>Implementation Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>In our company direct and indirect processes are well documented.</td>
<td></td>
</tr>
<tr>
<td>We continuously measure the quality of our processes by using process measures</td>
<td></td>
</tr>
<tr>
<td>(e.g. On-time-in-full delivery rate).</td>
<td></td>
</tr>
<tr>
<td>Our process measures are directly linked to our plant objectives.</td>
<td></td>
</tr>
<tr>
<td>In our company there are dedicated process owners who are responsible for</td>
<td></td>
</tr>
<tr>
<td>planning, management and improvement of their processes.</td>
<td></td>
</tr>
<tr>
<td>A large percentage of equipment on the shop floor is currently under statistical</td>
<td></td>
</tr>
<tr>
<td>process control (SPC).</td>
<td></td>
</tr>
<tr>
<td>We make use of statistical process control to reduce variances in processes.</td>
<td></td>
</tr>
<tr>
<td>For root cause analysis we have standardized tools to get a deeper understanding</td>
<td></td>
</tr>
<tr>
<td>of the influencing factors (e.g. DMAIC).</td>
<td></td>
</tr>
<tr>
<td>We operate with a high level of PAT implementation for real time process</td>
<td></td>
</tr>
<tr>
<td>monitoring and controlling.</td>
<td></td>
</tr>
</tbody>
</table>
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Summary & Outlook

- Quality Organizations have to be analysed using a systemic approach.
- An evaluation on individual KPI level has to be avoided
- Current initiatives like FDA Quality Metrics brings Quality and OPEX closer together
- The research of the University is showing the positive impact of Quality on overall OPEX performance
- Data becomes more and more mandatory for informed decisions about improvements on all levels of the organization
- Quality is the outcome of mastered processes – therefore process capability is an important indicator
- Quality is the foundation for superior OPEX performance!