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Capturing & Leveraging Diagnostics Information

Across the Pharmaceutical Plant

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FESTO

contents

Introduction

Information Is Control

You've heard the cliché before, "one can't manage what one doesn't measure." Fortunately the growing connectivity of plant and process systems, as well as the myriad controls associated with pharmaceutical manufacturing plant operations increasingly provide managers with the "measure" to evaluate all aspects of production. Especially relevant to safe, efficient, transparent and healthy operations is the diagnostic and other data generated by current-generation control devices. More recently, this connectivity has reached even further into process control with diagnostic data available from simple solenoid valves and other devices associated with the final control of skid mounted systems. To help managers understand more deeply the quality and risk management benefits that their connected control devices can bring, Festo presents this E-book to shine a light on the full-time value of real-time diagnostic data.

Improved Diagnostics from Decentralized Solenoid Valves and I/O Systems

By Craig Correia, Head of Process Automation, Festo Corporation

INFORMATION ABOUT the health of a control system, the I/O systems, field devices and final control elements can be critical for plant operation and uptime. Timely diagnostic information can mean the difference between a quick repair and hours or days of unplanned downtime. This is especially true of pneumatics and solenoid valves used as air pilots, which are often the forgotten parts of a modern control system.

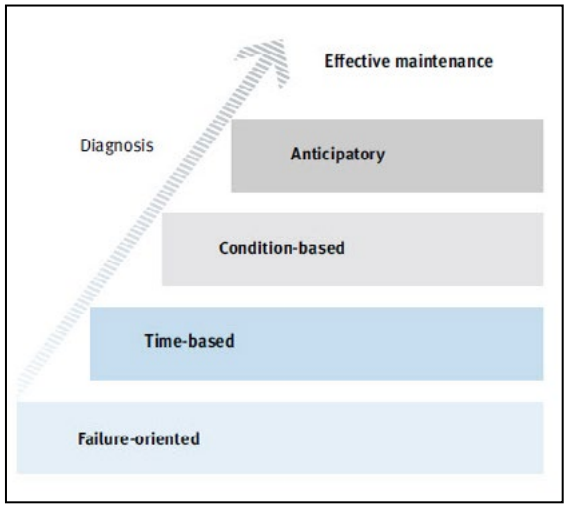
In the past, and in many plants even today, diagnostic information is captured in many ways, including manually, using clipboards, Excel spreadsheets, barcode readers, and by laptops carried into the plant. Much of this data winds up being unused and discarded. The information isn't available in real time to allow real time decision making on the part of operators, engineers, and maintenance managers.

THE CONNECTED PLANT

The concept of the Internet of Things, developed a decade ago by a group of visionary companies including Cisco, provides a way to think about organizing the information in a plant, from operating variables, maintenance, and diagnostic information.

Originally called Machine to Machine (or M2M) Communications, the Internet of Things posits that every sensor, every controller, and every final control element, whether valve or variable frequency drive, be connected in real time to every other

device on the manufacturing network, and from there to the rest of the plant and enterprise networks throughout the enterprise.



There are both benefits and negatives to the Internet of Things, as with most technological advances, but the benefit to manufacturing is that it is becoming almost ridiculously easy to connect all the devices in a plant to a real time network.

The minute you can get information from all the devices in a plant in real time, you have the ability to operate the plant, and maintain the plant in a significantly different way from the past. Real time operations data enables the plant to be "tuned" to operate in the most efficient or most profitable manner (they are not always the same) and provides the ability to apply the techniques of the other new information technology, Big Data. For maintenance and operations, being able to get information to and from all the devices in the plant in real time makes asset management practical in a whole new dimension.

BENEFITS OF ASSET MANAGEMENT

The basic benefits of asset management are clear. Proactive asset management can prevent extremely costly unplanned shutdowns. How costly is "extremely costly?" A catastrophic failure of a master pump in a refinery could cost not only the entire production of the refinery for the length of the downtime, but also additional costs from cascading failures of additional components. A failure of a temperature sensor in a biotech plant could cause the spoilage of literally millions of dollars worth of product. A missing additive in a batch, caused by the failure of a single solenoid valve, could result in scrapping the entire batch, at a cost of possibly millions again.

What you need to do is to see a failure coming, before it occurs. It is necessary to get the data in real time to be able to see those potential failures. The problem is that while that information does exist, getting it to plant operations and maintenance personnel in real time can be truly difficult.

PLANT HEALTH INTELLIGENCE

Information about the health of a control system, I/O module, even a field device, and sometimes including diagnostic events, is readily available through any DCS or PLC. But the use of diagnostics is only common when the controller and I/O subsystems are from the same manufacturer. In biotech or pharmaceutical installations, not to mention CPI and petrochemical applications this is not often the case.

In biotech and pharmaceutical applications, control cabinets, skids and even entire plant units are often procured from different machine builders or integrators. Each of these uses the sensors, valves and controllers that it has selected, unless the end user specifies otherwise. Therefore, most OEMs and integrators provide

their own preferred sensors, analog valves, solenoid valves and controllers.

Unfortunately, it is not easy to obtain diagnostic information from different control systems and different brands of I/O, a different bus, or different manufacturers of sensors and valves. Because it can be difficult to acquire this information, it is usually underutilized. Sometimes, operators and maintenance personnel don't even know that this diagnostic information exists.

This is especially true of pneumatically operated solenoid pilot valves. Control systems are optimized today for electronic devices. Pneumatic devices seem sometimes to be relics of another time. Yet solenoid air pilot valves, both centralized on a manifold or decentralized at the media valve, can provide quicker and more reliable control and their electrical brethren.

To be a world-class facility in the 21st century, all the field devices in the plant need to be connected to the control system and from the control system to the asset management software—including the pneumatic field devices like solenoid pilot valves.

PLANT NETWORKS AND FIELDBUS CONNECTIONS

Plants have moved decisively to a single network using Ethernet. This network can be wired or wireless using IEEE 802.11x. But this kind of network has only recently begun to penetrate to the device level. Instead, there are a number of device networks, called fieldbuses. These include Foundation Fieldbus, HART, Profibus, Profinet, Modbus, Ethernet/IP, DeviceNet, and several others.

Devices such as analog control valves, pneumatic valve terminals and field sensors are commonly connected via fieldbus and integrated into the plant controls, the same way I/O terminals and secondary controllers are. The challenge is not all of these devices offer diagnostic feedback or it is not being utilized.

For examples of how to integrate Festo CPX/MPA range and access diagnostic information from your controller, visit www.festo.us/biotech/diagnostics

Both PLC and DCS control system vendors such as Emerson Process Management and Rockwell Automation promote diagnostics based on asset management systems. It is possible to seamlessly interface any controller, I/O terminal, or pneumatic solenoid manifold into these systems but not all devices offer the same level of diagnostic feedback.

Emerson's CHARM I/O connects HART compatible field devices and communicates diagnostics back to the control system and the asset management system. Other Emerson I/O does the same for Foundation Fieldbus. But CHARMs are not designed to handle control and diagnostics of solenoid pilot valves mainly because for many valve manufacturers that technology is lagging.

Another common platform is Rockwell Automation's RSLogix systems which can connect with various brands of I/O and field devices using Ethernet/IP, but when you start talking about pneumatics valves the same issue arises. Similar to the Emerson example, manufacturer technology in most cases limits the functionality of pneumatic pilot valves to a simple on/off control.

The solution is to specify pneumatic solenoid valves with diagnostic capability, whether used for handling automation or piloting.

ADVENT OF DIAGNOSTICS ON SOLENOID AIR PILOT VALVES

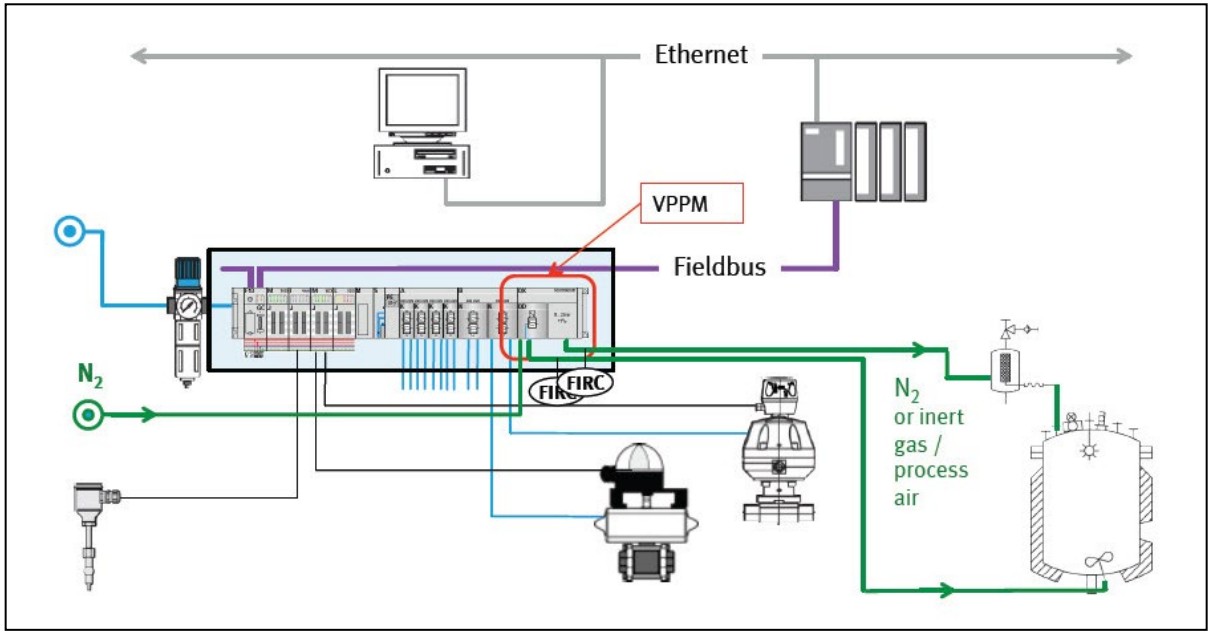
This is much more important than it may first sound. In a typical pharmaceutical plant doing API production, there may be literally thousands of solenoid pilot valves in control panels, mounted on machines, and mounted on walls. While a typical solenoid lasts seven to ten years in an API plant, if any one of these valves fails, there may be a cascading failure that may ruin the process or batch that is being run. Having predictive diagnostics on these valves might save thousands of dollars, or even more, in the event of failure.

It doesn't help to keep the plant from going off line you have all the analog sensors and all the analog control valves producing diagnostic information, but the diagnostics from your plant's population of solenoid air pilot valves can't be seen. What inevitably happens is that the solenoid valve will be the point of failure that shuts down the plant or the batch reactor train, or the entire process, because predictive maintenance cannot be applied if the diagnostics from the solenoid valve cannot be seen.

It is good practice, then, to purchase solenoid valves, I/O, and controllers that have rich diagnostics built in. In most control systems a pneumatic solenoid valve appears merely as a digital output and a local LED.

Pneumatic valve terminals are available today which can supply open load or coil current monitoring at the specific valve, pressure monitoring inside the valve terminal and even detect in a manual override has not been reset.

On the electrical side, the CPX terminal has combined five different I/O connection technologies for digital and analog I/O, and multiple I/P transducers can be mounted with the pneumatic valve and electrical I/O. Festo offers an option for IP20 high density digital I/O for cabinet installations, as well as the ability to support redundant bus control with



Example of Performance and Value: Versatile CPX/MPA integrated I/P is able to both pilot process valves and control inert gas flow directly to reactor vessels.

A solution is to consider the Festo CPX/MPA. This product will integrate with most leading PLC and DLC platforms and deliver uniform control and diagnostic information from the field, including I/O, I/P and pneumatic solenoid valves. The diagnostics is already built in due to an internal bus that runs thru the backplane of the pneumatics and I/O.

The Festo MPA series of solenoid valves offers full pneumatic diagnostics when used with the CPX controllers, including cycle count, line pressure, and failed solenoid indication. It also enables the designer to install up to 128 solenoids on a single manifold. This is four times the density of competitive manifolds. This reduces installation footprint, and more.

embedded controller and isolated power zones for safety.

Detailed diagnostic functions are needed to locate the causes of errors in the electrical installation and reduce plant downtime. The Festo design begins with optionally color-coding valves and LEDs, which Festo believes simplifies validation and troubleshooting. Festo calls this on-the-spot diagnostics. Further point diagnostics are available from the manifold, or through the bus connection to the control system via explicit messaging. Festo on-the-spot diagnostics include under voltage monitoring, fieldbus status, controller and I/P transducer status, and module specific diagnostics as well as valve-specific diagnostics and solenoid coil status.

Short circuit detection for sensors, outputs and valves is supported. Open load detection finds missing solenoid coils.

Festo's CPX series terminal also has on-board history, which can store the last 40 causes of errors, along with error start and end times.

Diagnostics can be also retrieved using a hand-held terminal, or by using Festo's maintenance tool software on a laptop, and are capable of being read out on the fieldbus interface and historicized to evaluate the causes of errors and failures. The series offers optional access via the integrated Ethernet interface for remote maintenance using PC or Web applications.

Selecting the Festo CPX series can provide a whole new level of diagnostics when the end user is specifying the I/O and solenoid air pilot valves for a skid or integration project.

DIAGNOSTICS AND THE CONNECTED PLANT

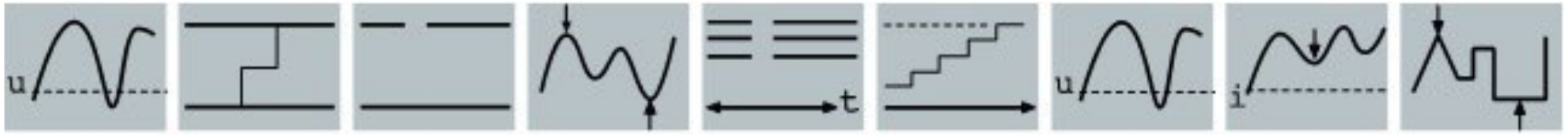
As the Internet of Things becomes more of a reality, and penetrates the industrial process and discrete manufacturing operations, the value of diagnostics will increase exponentially. Diagnostics will be critical to the acquisition of process data, and will provide the device health data that is necessary to fully enable predictive maintenance throughout the plant.

Most vendors of control systems have integrated diagnostics for electronic sensors and electronically-actuated control valves.

Simple on-off valves, like solenoid air pilot valves, have often been overlooked because it has been a standard assumption that these valves are not as important as control valves, or field sensors. Pneumatic solenoids have been bypassed or ignored for diagnostic purposes for years.

But this will need to change, as all of the sensors and field devices in a plant become connected and smart.

In the pharmaceuticals and biotech industries, validation and GMP issues have increased the demand for real-time diagnostic information. At the same time, the increasing use of skid-mounted production processes has made the use of dissimilar control systems a near certainty. This means that end users must insist on diagnostics in every I/O terminal, in every sensor, and in every final control element on their skid. I/O must have easy diagnostic information transfer using fieldbus. Festo's CPX/MPA series provides a way to produce that as a plant standard.



Undervoltage per module
- Electronics-25%.
- Load-10%.
- Emergency-stop s10v.

Short circuit selectable
- For each channel.
- For each module.
- For each valve.

Wire break selectable
- For each channel.
- For each module.
- For each valve.

Upper/lower limit value
- For each analogue channel.
- Voltage.
- Current.
- Temperature.

Error memory
- Last 40 messages.
- With a stamp.
- Recognizing of sporadic errors.

Condition monitoring
- Setpoint specification for each valve.
- Monitoring of down stream mechanics/ processes.
- Preventive diagnosis/ maintenance.

Undervoltage per valve manifold
- Additional supply for valves monitored separately.

Monitoring of space required control
- Pull current.
- Coil clamped.
- Manualoverride not reset.

Pressure-monitoring
- Threshhold value.
- Comparator.
- 16-bit numeric.

Learn how to calculate financial validation for migrating your legacy distributed control system to a new automation system.

HOW TO JUSTIFY DCS MIGRATION

By Mike Vernak, DCS Migrations Program Manager, Rockwell Automation

IMPLEMENTING A single control platform across all plant-floor applications provides you with a number of advantages, including reduced spare-parts requirements, more synchronized processes and lower maintenance and training costs. It also improves plantwide integration by enabling the seamless transfer of real-time data from disparate control systems for improved decision-making and increased manufacturing flexibility.

Many plants with process applications have an outdated distributed control system (DCS). As these systems reach the end of their useful life, migration to a new automation system is required. However, before this can take place, you must provide financial justification. This justification must compare the cost of continued DCS operation to the costs and benefits of migration to a new automation system — or the total cost of ownership (TCO) for each system. This is the most comprehensive way to analyze and justify a DCS migration project. TCO takes into account all relevant financial factors, including purchase price, maintenance costs, energy consumed, downtime and quality.

EVALUATING THE OLD SYSTEM

Excessive maintenance and support costs, along with high levels of downtime, are the most visible reasons to migrate from a DCS to a new automation system. They're also the easiest to quantify. Older DCSs can become expensive to operate and maintain for three reasons:

1. Increased system failure due to deteriorating components.
2. Difficulty procuring spare parts.
3. Lack of qualified maintenance staff.

All three of these, in addition to product changeovers, can cause excessive downtime and increased costs. This is a significant expense for continuous process operations because plants typically take hours or even days to restart after an interruption.

Harder to analyze are the costs associated with poor process control. Substandard process control results in

EXAMPLE OF AN NPV CALCULATION FOR A FIVE-YEAR PERIOD			
Net Present Value		Existing DCS	New Automation System
Interest or Discount Rate	6%		
Net Present Value		$560,483	$311,542
Year 1 TCO, investment plus savings minus costs		($100,000)	($850,000)
Year 2 TCO, savings minus costs		($110,000)	$150,000
Year 3 TCO, savings minus costs		($126,500)	$150,000
Year 4 TCO, savings minus costs		($151,800)	$150,000
Year 5 TCO, savings minus costs		($189,750)	$150,000

The most accurate financial analysis is to determine the net present value (NPV), which estimates the value of continuing with the existing DCS as opposed to the new automation system.

excessive energy use, poor quality and reduced throughput. Controlling the process tighter to set points helps maximize these components and minimize waste.

For example, heating a product to 0.1° over its set point consumes less energy than heating it to 2° over its set point. For plants running batch processes, adding too much of an ingredient can create an unacceptable product, and thus scrap. Even if the batch is acceptable, costs might be higher than needed if the ingredient is added in excess quantity.

It's also important to consider the system's level of integration with third-party hardware and software platforms. Older DCSs generally don't support modern, open communication standards, so it might not be possible to add needed features. With a new automation system, additional features can be built in or relatively simple to integrate.

NEW AUTOMATION SYSTEM COSTS

In addition to calculating the TCO, you also need to quantify new automation system costs and benefits. New system costs can be broken down into three main categories:

1. Installed cost of the new automation system.
2. Cost to train employees on the new system.
3. Downtime incurred while installing the new system.

The first two costs are generally straightforward to quantify because suppliers can give fixed-price quotes for each. The cost of downtime incurred while installing the new system is harder to quantify, but can be minimized by following a three-phase migration method. Breaking up the total required downtime into multiple periods often is advantageous and spreads migration costs out over a longer period.

In phase one, the most obsolete components — the human-machine interfaces (HMIs) — are converted first. This often can be performed with minimal downtime, and in some cases, none.

In phase two, the legacy process controllers are replaced while allowing processors to reuse existing I/O modules to maximize the return on their existing investment.

FAST, EASY INTEGRATION FOR A LEGACY DCS TO COMMUNICATE WITH CONTROLLOGIX PACS

Encompass Product Partners in the Rockwell Automation PartnerNetwork offer technologies that complement Rockwell Automation solutions and can help migrate your DCS. Learn more about these partners:

Molex: Migration solutions connecting to Modbus.
www.rockwellautomation.com/go/p-molex

Online Development, Inc. (OLDI): Migration solutions connecting to ABB Bailey Infi 90 or Network 90 DCS systems.
www.rockwellautomation.com/go/p-odi

Phoenix Digital:
Fiber solutions connecting to Honeywell DCS and Modbus.
www.rockwellautomation.com/go/p-phoenixdigital

ProSoft Technology:
Migration solutions connecting to Honeywell IPC-620 I/O bus, GE Genius Bus I/O (Taylor Remote I/O), and Fisher Provox Control I/O bus.
www.rockwellautomation.com/go/p-prosoft

In phase three, the I/O is replaced. In many cases, automation suppliers have wiring solutions that allow you to remove legacy I/O without the need to remove field wires, reducing installation costs and risks associated with I/O replacement.

FINANCIAL ANALYSIS

The final step in justifying the value of migration is a financial analysis. The most accurate financial metric is the net present value (NPV). The NPV estimates the value of continuing with the existing DCS as opposed to the new automation system. It also incorporates the interest rate, referred to as the corporate discount rate. The NPV can be difficult to quantify because it requires annual costs and savings for each option to be listed for the expected life of the shorter-lived option. For example, if the DCS will be obsolete and unsupportable in five years, then the annual TCO for the existing DCS and the new automation system would have to be calculated for each of the five years, with all values discounted back to the present. The table on previous page shows an example of an NPV calculation for a five-year period.

As the table shows, the existing DCS has an annual TCO of $100,000 that's increasing at a rate of 10% the first year, rising by 5% per year to 25% in the fifth and final year as the DCS becomes increasingly unsupportable. In the end, a new automation system would require an investment of $1,000,000, but would save $150,000 per year in TCO as compared to the existing DCS.

DO IT RIGHT

Comparing the TCO for the existing DCS to that of a new automation system indicates whether the migration is financially justifiable. Outside assistance sometimes is required to evaluate a prospective upgrade, and this can be provided by consultants, system integrators or automation suppliers. A good partner should be able to provide much of the data required, help you identify your needs and put together a migration plan based on your goals, constraints and future plans.

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Improving the Reliability of Physical Assets

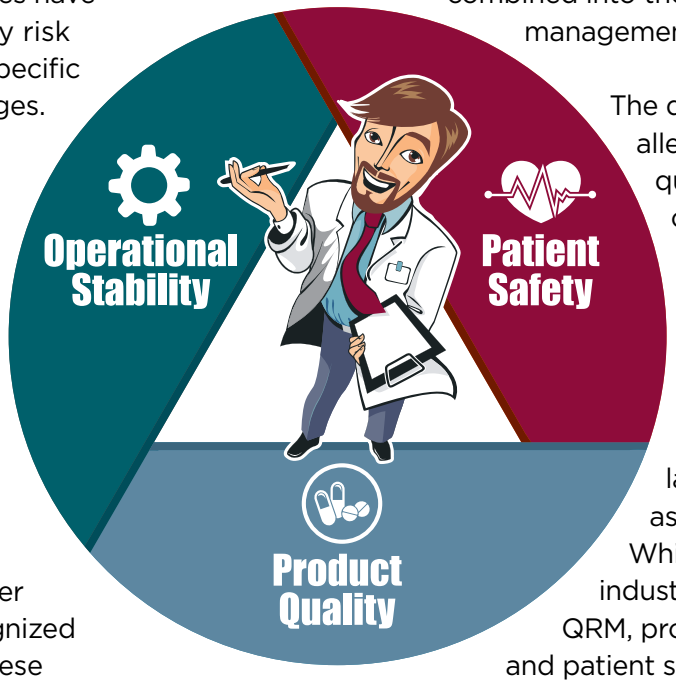
Risk-based asset management provides the foundation for operational stability, product quality and patient safety

By David J. Mierau, PE, CMRP, Life Cycle Engineering

RISK-BASED ASSET management policies and practices for physical assets are valuable additions to operations within the pharmaceutical industry. These practices have strong parallels to commonly used quality risk management (QRM) concepts, and have specific benefits related to preventing drug shortages. Specifically, risk-based asset management programs are intended to control risks associated with product manufacturing, packaging, facilities/utilities infrastructure and supply chain inventory management within controlled environments.

QUALITY RISK MANAGEMENT BACKGROUND

The pharmaceutical industry has been focused on the benefits of risk-based strategies for the past decade, with large-scale guidance on the topic published under ICH Q9[1]. Currently, there are multiple recognized international standards that incorporate these concepts such as ASTM E2500[2] and the ISPE Baseline Guide for Commissioning and Qualification[3]. The primary purpose of these standards is to provide requirements and guidance for balancing product quality, patient safety and financial cost. This focus has combined into the overarching concept of quality risk management (QRM) for the pharmaceutical industry.



The driving force for QRM is the need to alleviate the immense burden of validation, qualification and commissioning of systems associated with the development, manufacture and distribution of pharmaceutical products. Traditional methods of paper-based process and equipment validation efforts utilized prior to QRM required pharmaceutical companies to make large investments in time and labor for asset installations and modifications. While these costs are still significant for the industry, they have been reduced. Through QRM, processes that are critical to product quality and patient safety receive the most rigorous validation and care, while other non-critical systems may only require commissioning to ensure basic desired functionality.

While QRM has been a great advancement for maintaining product quality and alleviating some business burdens, it does not expand guidance to other critical aspects of the business such as production reliability and market delivery. To maintain a focus on patient safety but also ensure reliable delivery of products when they are needed, companies need to combine their current QRM policies with risk-based asset management principles. This combination provides the foundation for stabilizing production and supply chain operations, which allows for clear understanding of market delivery capabilities and early warning signs for drug shortages.

DRUG SHORTAGES

In October of 2013, FDA published a Strategic Plan for Preventing and Mitigating Drug Shortages in response to a new requirement within the Food and Drug Administration Safety and Innovation Act (FDASIA)[4]. Due to ongoing drug shortage events reported to FDA and the associated risk to patients, the Agency has been analyzing all facets of reliably delivering pharmaceutical products to the public.

Under the specific goals listed within the Strategic Plan, several tasks were identified to prevent and mitigate drug shortages. The following is an abbreviated list of those tasks that can benefit from risk-based asset management practices:

- Task 1.2: Improve Agency databases related to shortages and the tracking procedures FDA uses to manage shortages. Improved tracking will enable FDA to better assess progress on preventing and mitigating shortages.
- Task 1.3: Clarify roles/responsibilities of manufacturers by finalizing the proposed rule explaining when and how to notify FDA of a discontinuance or interruption in manufacturing, working with manufacturers on remediation efforts, and encouraging manufacturers to engage in best practices to avoid or mitigate shortages.
- Task 2.1: Identify ways FDA can implement positive incentives to promote and sustain manufacturing and product quality improvements.
- Task 2.2: Continue to develop risk-based approaches to identify early warning signals for manufacturing and quality problems to prevent supply disruptions.

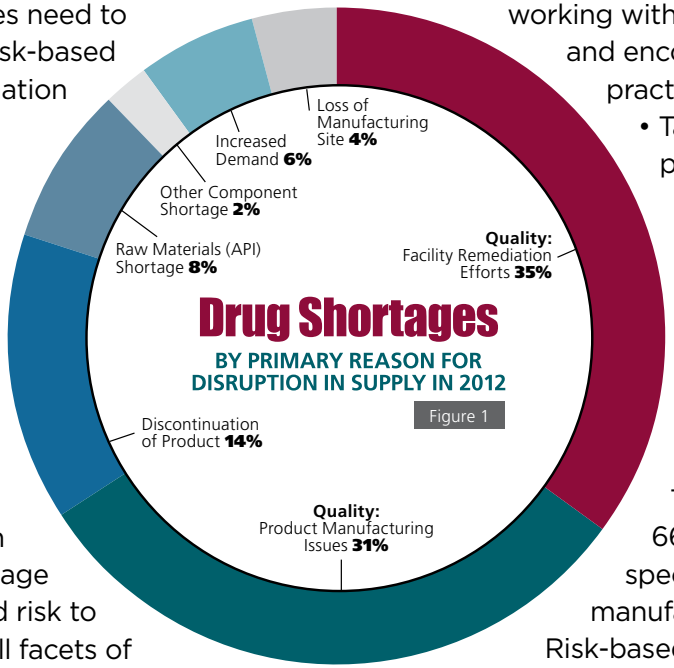


Figure 1

The data shown in Figure 1 indicates that 66% of disruptions are due to product-specific quality failures (31%) and issues with manufacturing processes or facilities (35%). Risk-based asset management practices can directly address these types of disruptions, and provide a better understanding of production demand concerns.

To further develop information regarding drug shortages, ISPE has developed a Drug Shortage Initiative Task Force to work closely with regulatory agencies and the pharmaceutical business community. The Task Force is comprised of industry representatives and they have been working on ways to better

understand the root causes and possible mitigations for drug shortages[5]. One example of this work is the Drug Shortages Survey issued in February of 2013 to professionals within different sectors of the pharmaceutical industry to collect more specific data regarding contributing factors to drug shortages. The results of this survey have been published by ISPE, and respondents identified that manufacturing quality issues were among the most prevalent causes leading to drug shortages, which is consistent with the information published by FDA[6].

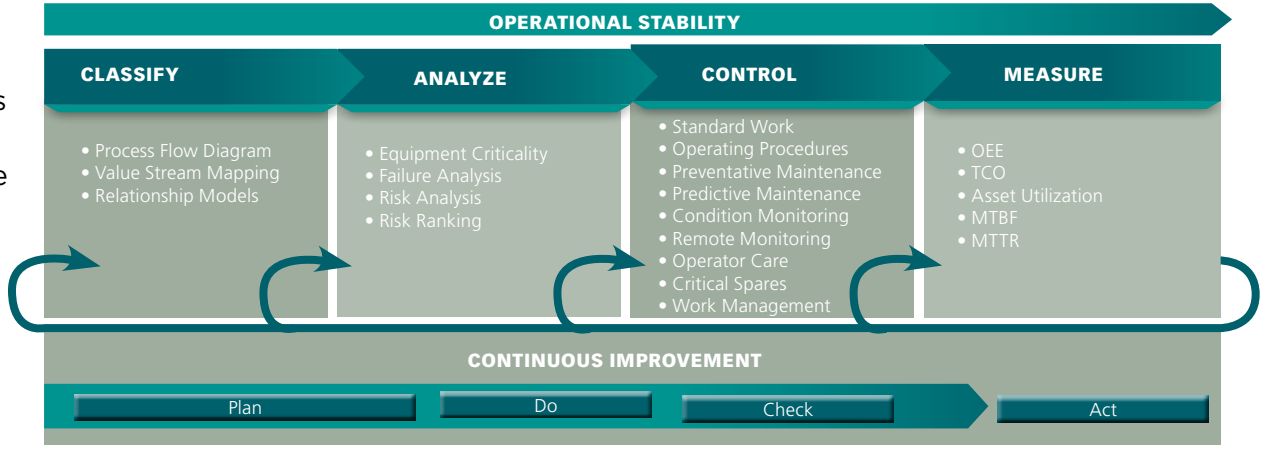


Figure 2: Risk-Based Asset Management Model

RISK-BASED ASSET MANAGEMENT

There are two primary recognized international standards regarding physical asset management: BSI PAS 55[7] and ISO 55000[8]. The current version of BSI PAS 55 was published in 2008, and ISO 55000 is currently in the final approval stage with expected publication in early 2014. These two standards are providing much-needed structure to the practice of managing physical assets, which is often loosely organized by ad hoc procedures, manufacturer-recommended maintenance practices, and a reactive culture where risks are not proactively analyzed or mitigated.

Both of these standards focus on managing physical assets across their entire life cycle, from concept to decommissioning, with guidance on effective asset management at each stage. The exact same risk assessment and risk management principles utilized by the pharmaceutical industry through QRM are applied within these standards. However, quality is only one component of overall asset criticality in a holistic management approach. Risk management methodologies have been successfully implemented within the pharmaceutical industry that still maintain focus on critical product quality and patient safety requirements, but also incorporate other risk categories such as:

- Safety (internal and external)
- Environmental
- Production Output (quantity)
- Business ($)
- Reliability (Mean time between failure, MTBF)
- Single Point of Failure (lack of continuity or contingency)
- Planned Utilization (%)
- Spare Part Lead Time (days)
- Maintenance Cost
- Decommissioning Cost
- Asset Replacement Cost

The criticality analysis, risk assessment and control strategy development process is just one aspect of risk-based asset management. Figure 2 represents

Asset Support	Asset Operation
• Organization Design • External/Contract Support • Procurement • Capital Project Management • IT Software & Infrastructure	• Compliance • Work Execution • Maintenance • Management of Change

Asset Utilization & Performance	Asset Improvement
• Planning & Scheduling • Subject Matter Expertise • Performance Monitoring • Performance Reporting	• Risk Assessment & Management • Reliability • Root Cause Failure Analysis • Continuous Improvement

Table 1. Aspects of Asset Management Program Organization

a model for risk-based asset management; note the overall goal of operational stability. Stable operations deliver consistently on schedule with minimal unexpected disruptions. Also, forecasting is much more accurate for a historically stable operation, providing less uncertainty around delivery of products to market.

The model in Figure 2 also separates activities into four phases: classify, analyze, control and measure. From an implementation perspective, this progression is ideal to establish the most effective asset management program: one where all risk control strategies are based upon specific asset failure modes. Continuous improvement through monitoring of key performance indicators is also a key feature of this model.

Based upon the structure presented within ISO 55000, other aspects of an asset management program can be organized into the following categories as seen in Table 1.

DRUG SHORTAGE PREVENTION PROGRAM

While there are many complex aspects of pharmaceutical production and distribution that ultimately must be incorporated into a complete Drug Shortage Prevention Program, Figure 3 represents a high-level structure from the manufacturing organization perspective:

The QRM element is comprised of the traditional Quality Assurance and Quality Control aspects of pharmaceutical manufacturing. Quality Assurance is the standards, policies, procedures and processes designed to deliver consistent, safe, high-quality products. Quality Control is the product sampling and testing division of Quality that exists primarily for intermediate and final product release verifying a product meets safety, identify, strength, purity and quality (SISPQ) requirements.

The Safety & Environmental Element incorporates the aspects of federal and local regulatory compliance requirements. This is an essential component of the Drug Shortage Prevention Program because even though a process may be producing quality product, it could be shut down due to significant safety or environmental concerns that outweigh the impact of stopping production.

Asset risk management, as described under risk-based asset management previously, is a key element to preventing drug shortages because it essentially defines what quantity of product can and will be produced. Holistic asset risk management also incorporates the elements of QRM, Safety & Environmental into implementation as well. For performance monitoring, asset utilization is a fundamental indicator of asset management from a production perspective: This indicates what percentage of assets are functioning over available production time. Overall

PROGRAM ELEMENTS	ELEMENT REQUIREMENTS	DESIRED OUTCOME	AGENCY DATA REPORTING
Quality Risk Management	Quality Assurance Quality Control	Patient Safety	Nonconformance Trends & Recalls
Safety & Environmental Risk Management	On & Off-Site Compliance	Personnel & Community Safety	Significant Events
Asset Risk Management	Failure Mode Based Risk Control Strategies	Stable Operations & Cost	Asset Utilization OEE Trends
Supply Chain Risk Management	Inventory & Logistics Risk Mitigation	Predictable Demand Realization	Inventory Trends Missed Orders

Figure 3: Drug Shortage Prevention Program Structure for Manufacturing

equipment effectiveness (OEE) is a combination of quality, rate and availability from the operation. While this performance indicator is typically low for the pharmaceutical industry (20-30%), trending this combines multiple aspects of production concurrently and is an excellent high-level monitoring metric.

Supply chain risk management within the manufacturing boundary is a key element of operational reliability as well. Raw products, inventory management and warehousing all have significant potential impact on drug product delivery. The supply chain and asset risk management processes and procedures must be closely aligned to ensure production systems work well together.

Agency Data Reporting as represented in the structure indicates the information that would be included in regulatory agency databases to monitor product delivery. Utilizing a dashboard type of communication, agencies can be notified of negative performance trends in quality, safety, asset performance or supply chain delivery. Manufacturers would also be monitoring trends prior to data submission, and can provide explanations and action plans where appropriate to address negative trends. Consistent or positive

Source: FDA Strategic Plan for Preventing and Mitigating Drug Shortages

Task	Task Description	Risk-based Asset Management Actions
1.2	Improve Agency databases related to shortages and the tracking procedures FDA uses to manage shortages. Improved tracking will enable FDA to better assess progress on preventing and mitigating shortages.	Manufacturers shall report Asset Utilization and OEE to Agency databases for trending. These metrics will indicate what percentage of the maximum production capacity is being manufactured.
1.3	Clarify roles/responsibilities of manufacturers by finalizing the proposed rule explaining when and how to notify FDA of a discontinuance or interruption in manufacturing, working with manufacturers on remediation efforts, and encouraging manufacturers to engage in best practices to avoid or mitigate shortages.	Best practices shall include a holistic risk-based asset management program based upon established international standards such as BSI PAS 55 or ISO 55000.
2.1	Identify ways FDA can implement positive incentives to promote and sustain manufacturing and product quality improvements.	By trending Asset Utilization and OEE, manufacturers can be rewarded based upon consistent delivery, delivery on forecast, and positive trends where warranted by the market.
2.2	Continue to develop risk-based approaches to identify early warning signals for manufacturing and quality problems to prevent supply disruptions.	Utilize performance measurement data from the risk-based asset management program as leading indicators for supply disruptions. A negative trend in OEE against increasing market demand would be an early warning example.

Table 2. Tasks Addressed Through Risk-Based Asset Management

performance that is trending in-line with product demand from the market would not require specific review or explanations.

PREVENTION PROGRAM BENEFITS

From the FDA Strategic Plan for Preventing and Mitigating Drug Shortages, the identified tasks can be addressed through risk-based asset management with the actions shown in Table 2.

Preventing drug shortages is about effectively managing risks and utilizing data-based leading indicators to generate warnings early enough to take corrective or mitigating actions. While the overall supply chain will present added complexities from wholesalers, pharmacies, hospitals and healthcare providers, the Drug Shortage Prevention Program structure proposed brings forward key benefits of focusing on risk-based asset management. Improving the reliability of physical assets provides the foundation for operational stability, maintains a focus on product quality and patient safety, while addressing the manufacturing risks associated with drug shortages.

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