



Health Sciences

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THIS IS YOUR TIME TO...

Start, Stop, Do More, Do Less

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welcome

A warm welcome to 2020 from all of your friends and colleagues at NSF. Although this issue will reach you a month or so after the New Year festivities, it coincides with a critical time of year for us all – the first financial quarter!

We realize that all successful businesses strive for a fast start, to get ahead of plans and schedules and to complete commitments on time in full. There's no better feeling than a good start to the year and we want to help you survive, thrive and get ahead of your competition in what is an increasingly volatile, unpredictable, complex and ambiguous business environment. To succeed, the key steps are clear:

1. Research options
2. Evaluate risk and reward
3. Plan and make commitments
4. Integrate your resources, engaging the whole workforce in the improvement
5. Follow through with those commitments
6. Evaluate the level of success achieved and share the learnings

Speaking with John Johnson recently, he reminded me of his secret for a successful marriage and it wasn't roses and prosecco! Each quarter, starting this time of year, he sits face to face with his wife and reflects on what's happening around them and they agree together:

- > **What to start doing**
- > **What to do more of**
- > **What to stop doing!**
- > **What to do less of**

Likewise, sharing the realities of life, speaking the unvarnished truths and plotting a future that works for the organization and for the individuals within it, is a key attribute of successful companies.

We have some great articles on the critical process of turning strategy into action (see article on the facing page) and we have grouped our key articles according to what we would recommend you start doing, stop doing, do more of, or do less of.

Of course, this edition is also crammed with information about the industry around us, the key trends and indicators, our life at NSF and your life in the wonderful world of global health sciences!

Hope you enjoy it and don't forget to contact us if you need a little guidance as you enact the changes you desire throughout 2020.



Martin Lush



Martin Lush,
Global Vice President, Pharmaceutical Services
and Medical Devices, NSF International



How Do I Turn Vision Into Strategy and Strategy Into Action?

This time of year, many firms look to map out priorities for the coming year, but fall into the trap of acting first and thinking later.

We have studied the most successful pharma companies to discover key themes on why they are so good at converting their aspirations into a vision, their vision into a strategy and their strategy into actions.

What's more, they make those actions seem exciting, meaningful and worthwhile not just to the individuals performing the actions but also the wider organization. So how do you as a leader in your organization make the work ahead more meaningful?

The first step is to define carefully and succinctly what you want to be remembered for and what would characterize your team as the best it can be. Research what similar groups aspire to, but define your own vision.

The next step is to define your values and how you want others to see you.

This requires seeing the world as **it really is**, which can be difficult. This is why a well-structured, objective pharmaceutical quality system is so important. As shown below, GMP can define the key processes but don't forget the effect of culture and mindset. Being able to call out what is unacceptable (and to back it up with fact rather than opinion) is critical.

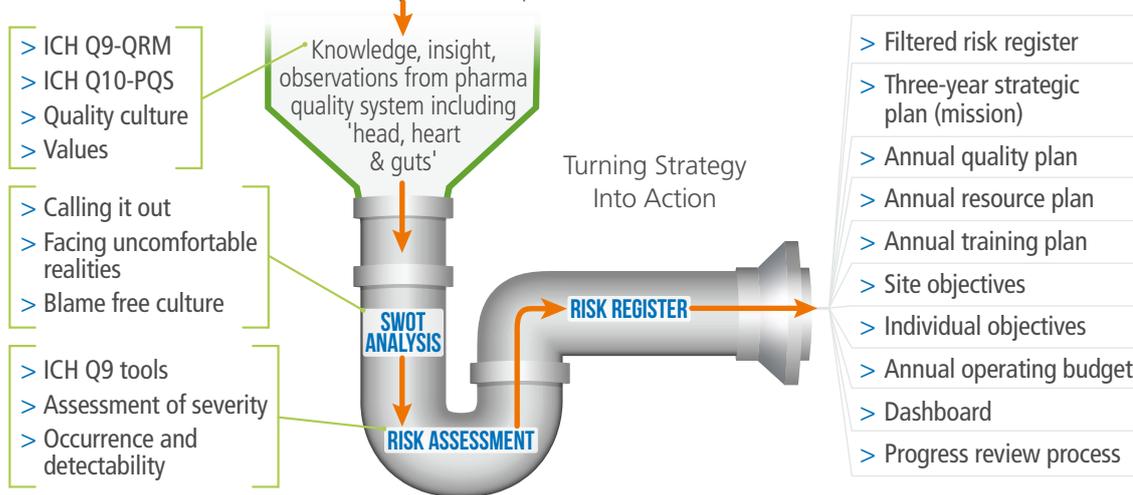
It's then easy to apply ICH Q9 to the known risks and to set a priority score that drives the organization's long-term strategy, which then defines short-term goals and individual objectives.

So how do you know how well your organization rates? How many outputs from this process are in place, meaningful, unambiguous and engaging to you? How many of those outputs are actively driving change and improving business performance?



by John Johnson, Vice President, Pharmaceutical Services, NSF International

What is my vision for the organization? | What do I want us to be?
 What do our clients and partners expect us to be?



If enthusiasm and engagement is in short supply, it's time to be concerned. If you need some guidance on how to do this, NSF experts will be happy to help you get the most from your team and its available resources.

Roald Dahl's 'My Uncle Oswald'

"I began to realize how important it was to be an enthusiast in life. He taught me that if you are interested in something, no matter what it is, go at it at full speed ahead. Embrace it with both arms, hug it, love it, and above all become passionate about it. Lukewarm is no good. Hot is no good either. White hot and passionate is the only thing to be."

▶ START

Using the Available Technology



by John Johnson,
Vice President,
Pharmaceutical
Services, NSF
International

Following this edition's theme of start doing, stop doing, do more of and do less of, isn't it time **to start** using the available technology to reduce error and deviation and **start a project to introduce electronic batch instructions and records?**

We are constantly researching and engaging with other industries, learning how they became successful, deep diving into the technologies, systems and behaviors that make the world's best companies more successful.

One aspect that comes up constantly is that other industries are deploying new technologies and applications faster than we are in the pharma industry. Of course there are notable exceptions, and some of our leading multi-nationals have deployed systems like quality by design, LIMs, e-QMS and electronic batch instructions and records (EBIR), but it is still notable that across the world many of our clients are using paper-based systems and minimal modern technology across the factory. There are several reasons for this, but do any of those reasons outweigh the huge benefits to GMP compliance, right first time, data integrity and adherence to standard

instructions? Why is our industry lagging in deploying modern technology in key areas, and isn't 2020 a good time to start to consider researching what options are available to define, control, monitor, automate and record our production and quality processes?

Providing it is defined and deployed carefully and with intensive user input, the use of EBIR can be transformational to your business. NSF worked with a client recently to transform the paper-based SOP system to a video link tablet-based system with great effect. We are also researching how Google's smartglass solutions could be deployed to define and monitor pharma processes.

Tony Margetts from FactoryTalk describes alongside how EBIR can be used to transform performance and compliance in pharma processes.



Electronic Work Instructions: A User Case for New Manufacturing App Technology

What Are Electronic Work Instructions?

Electronic work instructions (EWI) help eliminate paper procedures and forms on the shop floor to improve standardization, enable stronger operator guidance, and speed up and increase the accuracy of manual activities in production areas. Manufacturing applications (apps) are web-based software tools that are easily and rapidly configured to model process steps and sequences without the need for a large and costly IT system implementation and they do not require software development.

Apps are made available through tablet computers. These can be easily taken onto the shop floor and make use of simple dialogs and user interaction to record data that allow for greater visibility of the operation to other operators and managers. Any issues and errors can be dealt with immediately and notifications are built in using email for automating communication around the factory.

Advantages/Objectives of Using EWI

EWI have already been widely used across various industries, and:

- > Provide clear and repeatable instructions to operators
- > Allow efficient update of procedures by online collaboration and using good document practice
- > Ensure the latest instructions are being used and distributed across the facility
- > Can include content rich multimedia (e.g. photos, video, audio) in the instructions
- > Improve collaboration between operators, engineering teams and management
- > Communicate changes immediately
- > Are easily extended for adopting a culture of continuous improvement
- > Correct errors in real time
- > Collect data easily and make this available to all in dashboard and analytics
- > Allow real-time audits
- > Easily create effective training material
- > Greatly reduce training time
- > Reduce waste, errors and delays in manual operations

The pharmaceutical industry has been slow in picking up advances in the IT area because of concerns about change management and compliance with regulations. EWI represent a clear improvement in ways of working which do not conflict with the regulations if they are deployed in a controlled manner. It is possible to start with existing approved instructions (SOPs), systemize these and extend with additional content using collaboration and good document practice.

In training, EWI provide stronger guidance and are more intuitive and quicker to train new staff using interactive apps than with paper. The tool used for training is the same as that found in production, so training is hands-on and closer to real life, but training can be done offline before progressing to working in production with more experienced staff able to easily watch what is happening.



by Tony Margetts,
Principle Consultant
at Factorytalk Co.,
Ltd

How Do EWIs Fit Into the Existing Landscape?

Much of the software in today's factories is static. An example is an ERP system developed by an outside company to work in a broad range of factories. It is implemented from the top down by executives who know software can help, but don't know how best to adopt it. It may take three years to deploy all the planned functionality, and the result is often that users get screens that everyone isn't really happy with because they solve yesterday's problems.

Manufacturing apps provide a different, bottom-up approach that is solely aimed at rapidly bringing what the operators on the shop floor actually need: a configurable manufacturing platform that connects people, machines and sensors to help optimize processes. They can be deployed in a highly flexible manner allowing apps to be installed at just one workstation to gain immediate benefits and then be scaled up and out as needed.

Summary

EWI apps are an engine for manufacturing improvement and a major advance with a number of important consequences for production operations:

- > Apps offer a refreshing and flexible bottom-up approach to IT as a low-cost solution to focus on helping operators do a better job without mistakes.
- > Apps are designed to be human friendly to guide and report on important operations in a way that fits into the workflow.
- > The apps guide operators and record all needed actions electronically with automatic time stamps and audit trails.
- > Process information recorded can be extended to include live photos and video so more complete data can be captured.
- > Managers can monitor data in dashboards, see the current status of important processes and better communicate with their operators through electronic means without having to constantly be available on the line.
- > Defects and mistakes are captured in real time and can be corrected before they result in waste.
- > Apps can be deployed in days at lower cost than existing manufacturing IT solutions to bring and demonstrate benefits quickly.
- > EWI apps are simple and intuitive and built with building blocks like PowerPoint. They are version controlled and distributed to stations on the production line.
- > Typical improvements are:
 - Increased right first time by reporting defects at the source
 - Higher throughput
 - Standardization of manual processes
 - Faster training times
 - Real-time reporting on KPIs

In conclusion, manufacturing apps help to build quality in without the need for total automation so manufacturers can continue to best utilize people to optimize their processes. In the Industry 4.0 age, empowering the workforce is a critical aspect of digitization.

So, our question remains, you wouldn't use a mobile phone designed 20 years ago (or even two years ago), so why not start employing new technologies to solve age old issues? The millennial generation will demand new ways of learning, new ways of adding value and new methods of automating repetitive processes, so perhaps it's time to **start looking at new technologies.**

STOP

Hiding Quality Issues

We asked NSF’s Rachel Carmichael “What would you love to see the industry **STOP** doing in 2020?”

Her answer was clear: **STOP** using ICH Q9 to hide quality issues.



by Rachel Carmichael, Pharmaceutical Services, NSF International

Compliance to ICH Q9 Quality Risk Management (QRM) became a mandatory requirement in the EU, when it was adopted into EU GMP Chapter 1. Companies were expected to identify and understand their risks, and ensure the appropriate technical and organizational controls are in place to minimize the potential impact on patients.

Most companies introduced a formal risk management process, yet very few actually changed the way they operate, thus failing to become more proactive in addressing problems.

QRM has been raised as a topic regularly at MHRA GMP symposia, yet at the recent GDP Symposium in Glasgow, Alan Bentley (Senior GDP Inspector), described risk-based activities as “something that goes spectacularly wrong at times.” What’s going wrong?

A QRM system depends on:

- > Formalized procedures
- > Trained **and competent** personnel
- > Specific written instructions for the actual activities being undertaken
- > A strong methodology with clear criteria for scoring of risk
- > A reporting process

NSF has experience of companies that have conducted hundreds of risk assessments but failed to do anything *at all* with the output. It has been filed and forgotten rather than being used to steer the assessors to consider actions to reduce or eliminate risk and to balance benefits, risks and resources. There should be a clear and timely communication and escalation route for risk assessments within the company. Just because data is there, in a shared drive, it does not mean it has been communicated. We may have formed our message and transmitted

it but there needs to be someone to receive it and make sense of it. Risk assessments have become a source of bureaucratic inaction.

Weak methodologies can be behind some spectacular failures. Some systems appear to be deliberately designed to ensure that no action would ever be required! You could never score high enough numbers to warrant action, which is obviously of no use to anyone.

In 2013, WHO issued the draft document, Deviation Handling and Quality Risk Management, relating to deviations and QRM for the manufacture of prequalified vaccines for supply to United Nations agencies. The scoring system is worth considering as it ensures that potentially serious issues cannot be ignored.

SEVERITY SCORES (WHO):

SEVERITY	(S)	DESCRIPTION
Low	2	Minor GMP non-compliance; no possible impact on patient, yield or production capability
Moderate	4	More than one minor GMP non-compliance; possible impact on patient; moderate impact on yield or production capability
High	6	Major GMP non-compliance; probable impact on patient; high impact on yield or production capability
Critical	54	Serious GMP non-compliance; probable serious harm or death; critical impact on yield or production capability

OCCURRENCE SCORES (WHO):

OCCURRENCE	(O)	DESCRIPTION
Extremely low	2	Highly improbable to occur
Low	4	Improbable to occur
Moderate	6	Probable to occur
High	8	Highly probable to occur

DETECTABILITY SCORES (WHO):

DETECTABILITY	(D)	DESCRIPTION
High	2	Control system in place has a high probability of detecting the defect or its effects.
Moderate	4	Control system in place could detect the defect or its effects.
Low	6	Control system in place has a low probability of detecting the defect or its effects.
Non existent	8	There is no control system to detect the defect.

As with all FMEA systems, the risk prioritization number (RPN) is SxOxD, and risk is classified as:

High if > or equal to 216

Medium if >40 and <216

Low if ≤40

Let us consider an event where a complaint is received for a sterile liquid in a glass container, capped with a non-integral container closure. It is a repeat event (noted on 1,500 occasions in the last four years). Purely at the gut feel level it cannot be ignored. Using the WHO methodology, you could identify the scoring as:

Severity, critical (54), serious GMP non-compliance; probably serious harm or death; critical impact on yield or production capability.

Occurrence, moderate (6), probable to occur, may happen.

Detectability, moderate (4), control system in place could detect the defect or its effects.

So, the RPN would be 1,296 so easily classified as critical.

Using some basic scoring systems of risk (3, 2 or 1) could allow this issue not to be classified as high and an important opportunity to seek improvement could be missed.

Looking more closely:

SEVERITY – BASIC SCORES

- 1 Minor GxP non-compliance – no potential impact on product or patient, yield or production capability
- 2 Significant GxP non-compliance, potential impact on patient; moderate impact on yield or production capability
- 3 Serious GxP non-compliance. Probable serious harm or death, critical impact on yield or production capability

OCCURRENCE – BASIC SCORES

- 1 Improbable to occur. Rare event – <1% of units from a batch
- 2 Probable to occur. May happen – <10% of units from a batch
- 3 Highly probable to occur. Realistic chance/expected to happen. > 10% of units from a batch

DETECTABILITY – BASIC SCORES

- 1 Control system in place has a high probability of detecting the defect or its effects.
- 2 Control system in place could detect the defect or its effects.
- 3 There is no control system to detect the defect.

Severity should be very high (scoring 3), as it is a potentially leaking sterile product in the marketplace.

Occurrence – 1,500 over four years, 0.4% of our 375,000 units a year could score 1.

Detectability is not easy to see before shipping but there is a check in place so there is a system (scoring 2).

So, the RPN (SxOxD) could be just 6 which is unlikely to raise the required red flags that this example should warrant.

If your methodology could allow potentially critically flawed product to be ignored, it is time to consider your approach. FMEA may not achieve the desired outcome.

In conclusion it is time to **STOP** using ICH Q9 to obscure or downgrade issues, or to justify the indefensible or inaction. Please make 2020 the year you **STOP** using ICH Q9 to hide quality issues in your organization. Contact us at pharmamail@nsf.org with any questions.

III MORE

Create More Expert Quality Leaders

One thing is for sure this year – we will need more *expert* leadership to navigate the many challenges and create opportunities.

At NSF we work closely with leadership at every level, especially with Quality Directors. So, I asked the team: “*What’s the difference between leaders who excel and those who just get by?*”

Four key characteristics of successful leaders stick out. Our call to action to you is to explore how you and your team can do MORE in each of these areas.

1: GOOD UNDERSTANDING OF THE BUSINESS, NOT JUST QUALITY AND COMPLIANCE

How successful leaders think

- > They have a strong sense of “why,” beyond their job description, that inspires themselves and others. This starts with giving everyone a why (THE PATIENT), not just “because GMP compliance says so.”
- > The best QA leaders have usually experienced life outside QA, giving them a broad understanding of the business, the challenges, the pain points and the power of collaboration. They understand the full product lifecycle from R&D to manufacturing, operations, logistics and supply chain.
- > Their business knowledge allows them to think strategically, not just tactically.
- > They focus on future challenges like “What impact will regulation X have?”, “How will I manage 30% reduction in my budget over the next three years?”, “What impact will technology Y have in three years” and “What are my group’s succession plans for the next three to five years?”
- > They are prevention focused and consider crisis management and firefighting to be a sign of poor leadership and lack of strategic thinking.

How they act

- > Create rich networks inside and outside their business, driven by the desire to help others
- > Speak the language of business, not just compliance; they are business and financially literate

Additional Resources

Ted Talk: Start With Why by Simon Sinek

Book: Give and Take: Why Helping Others Drives Our Success by Adam Grant

2: JACK OF ALL TRADES – MASTER OF NONE

How successful leaders think

- > They don’t expect to know the answer to every question or to solve every problem. If they thought they could, they know they would be deluding themselves.
- > Their broad understanding of the business allows them to see patterns before problems occur.
- > They are comfortable with uncertainty. As one great leader said, “Not knowing everything is OK, it’s the ability to ask the right question, to the right person in the right way that matters. Then to pause, genuinely listen and then question again, and again and...”

How they act

- > Have five to six accurate and reliable key performance indicators (and surveillance systems) to allow assessment of controls, all leading, not lagging indicators.



by Martin Lush,
Global Vice
President,
Pharmaceutical
Services and
Medical Devices,
NSF International

- > Do less and then obsess. They practice the 80:20 principle, focussing 80% of their time on the 20% that matters – prevention, growth and improvement in things like:
 - People development
 - Simplification
 - Building and maintaining networks
- > Are passionate coaches and mentors who genuinely care for the development of the team.
- > Are resilient and future focused and:
 - Never accept the status quo
 - Thrive on failure (FAIL = first attempt in learning)
 - View complacency as the biggest threat to their company’s future.
 - Never take criticism personally
 - Consider organizational agility to be more important than productivity
 - Are obsessed by simplification and the KISS principle (Keep It Simple, Stupid). After all, agility and simplification go hand in hand. You can’t have one without the other.
 - Make sure their Deviation and CAPA, Change Control and Audit and Self Inspection systems focus on removing complexity, not adding it.
 - Practice NSFs Simplification Process!

Additional Resources on NSF’s Website

Webinar: The Tyranny of Key Performance Indicators

White Paper: Are You Facing a Complexity Crisis

Webinar: The Art and Science of Simplification – How to Win Your War on Complexity

White Paper: Changing Your Quality Culture and Improving GMP Behaviors: What Works and What Doesn’t

White Paper: How to Use B = M.A.t.H

Video: How to Jumpstart Your Pharma Business by Simplifying Processes

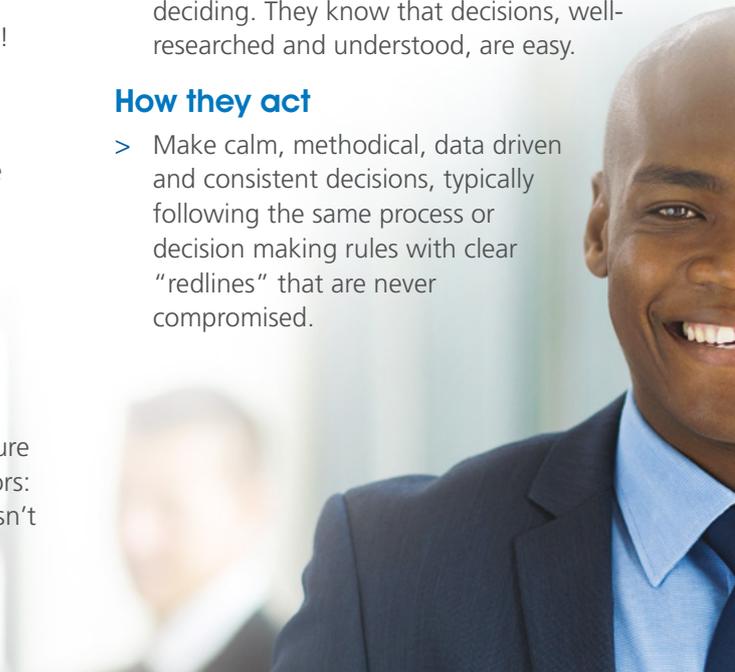
3: EXCELLENT RISK-BASED DECISION MAKING AND COMFORT WITH “LIFE IN THE GREY ZONE”

How successful leaders think

- > They recognize there is no such things as 100% compliance or zero risk.
- > They avoid paralysis by analysis (over-thinking).
- > They acknowledge that risk aversion creates more risk by adding complexity and diluting accountability.
- > By taking the 80:20 approach, they avoid decision making fatigue.
- > When making decisions, they put logic (data), before emotion or gut feel (which is wrong 80% of the time).
- > They think collaboration and consultation before deciding. They know more brains come up with a better decision and more accurate risk assessments. They rarely make a decision in isolation.
- > They are comfortable with constructive disagreements to challenge their understanding. They openly explore areas of disagreement to find a third way, rather than defend their position.
- > They focus on understanding before deciding. They know that decisions, well-researched and understood, are easy.

How they act

- > Make calm, methodical, data driven and consistent decisions, typically following the same process or decision making rules with clear “redlines” that are never compromised.



These include:

- I will never compromise patient safety.
 - I will never make a decision with a high level of uncertainty.
 - I will never decide purely on gut feel.
 - I will never succumb to group think.
- > Create space (time) between the event and the decision. The more important the decision, the bigger the space. They never make rash decisions.
 - > Consult widely before making important decisions, 80% listening, 20% questioning. They seek first to understand, before being understood.
 - > Avoid “yes” people, preferring to seek out those who will challenge them.
 - > Always review their decisions afterwards. “Was it right or wrong?”, “What would I do differently next time?”

Additional Resources on NSF’s Website

Webinar: Judgement Calls – Making Decisions Under Pressure

4: PASSIONATE COACH, MENTOR, TEACHER, LIFELONG LEARNER AND DELEGATOR

How successful leaders think

- > They believe they have an obligation to help and develop others and themselves, share knowledge and admit their mistakes. The job of any leader is to create leaders, so they walk the talk and model the way.
- > They recruit based on character and talent, not knowledge or qualifications. When you get people with the right character and talent – you can teach the rest.

- > They recruit “rebels” – people who think differently and have the courage to say there is a better way, and create an environment where this is possible.
- > When faced with a challenge, they consider whether it is a development opportunity, for themselves and their team.

How they act

- > Pursue education outside the classroom using the 10/20/70 method.
- > Delegate, coach and mentor relentlessly.
- > Create a rich learning environment where problems, unplanned events and crisis never go to waste. Every problem is seen as a learning opportunity. They openly share their failures (and learning) throughout the organization.

Additional Resources on NSF’s Website

Webinar: Training – Making it Stick

Also see my post on LinkedIn:

The Surprising Truth About Making Mistakes

What Next for 2020?

- > Discuss these characteristics with your colleagues – how do you and others compare? Do you think and act the same? What do you need to do **MORE** of?
- > Take advantage of the additional resources.
- > Please let me know what you think (martinlush@nsf.org) – I’m sure you can add to the list based on your own experiences.

Want to Accelerate Your Leadership and Personal Development?

Contact Martin Lush for a free and confidential chat, 1:1 coaching and mentorship. He has over 42 years’ experience and has held leadership positions from the shop floor to director level. He currently helps leaders at every level maximize their potential.



III MORE

Create A Quality Mindset



by Maxine Fritz,
Executive Vice
President,
Pharmaceutical
Services, NSF
International

Sometimes, to achieve MORE leadership, risk management and coaching, you first have to create a new mindset. Maxine Fritz explains how you can achieve MORE by adopting a quality mindset...

In the pharma industry, old mindsets can be hard to break. The perception has long been that quality is born out of compliance. Today's business environment offers another perspective. Over the past 10 years, the industry has dramatically changed due to globalization, increased competition, cost constraints, demands for efficiency, supply chain complexity and processes, and product complexity. Consequently, the industry's approach to quality must adapt as well.

Instead of asking what the minimal requirements are for regulatory compliance, the question should be how to improve quality holistically as an organization. A pharma company needs to think in terms of minimizing inconsistencies early and often throughout the manufacturing and business process. It must take on a quality mindset to compete and prosper.

The Old Mindset: *"Good compliance always translates to good quality."*

Regulations are a good starting point in that they meet minimal requirements. They should not represent a company's mindset in terms of quality. In fact, quality issues – not regulations – account for two-thirds of drug shortages.

The upfront costs of having a quality mindset can seem expensive. Yet in the long term, it is less expensive than having to address a compliance issue. At the low end, a regulatory action can cost a company over \$1 million dollars (or more if products are exported) of interrupted supply or remediation effort.

The Old Mindset: *"We don't have the size of organization to support a proper quality system."*

A quality mindset is an approach, not a department. It is a mentality that should exist and be practiced at every level. Instead of dwelling on the symptoms of an issue, a quality mindset addresses the source. The goal is to continuously identify and correct root causes of problems by:

- > Focusing on quality prior to compliance or enforcement
- > Maintaining data integrity
- > Taking measures to reduce human error
- > Investing in aging facilities, utilities and equipment

A company can invest in quality now, which inevitably leads to compliance anyway, or spend millions trying to correct problems later.

The Old Mindset: *"Process improvements work better in theory."*

For any leader, flawless execution should always be the objective to sustain a quality mindset. They need to understand that process improvement systems, like Six Sigma, are a means rather than an end.

In addition to improving product quality, compliance and the bottom line, Six Sigma can help companies focus on the building blocks that make up the quality mindset. These include:

- > Understanding human error
- > Evaluating data integrity problems
- > Optimizing processes
- > Understanding the reasons for poor quality
- > Preparing for inspections
- > Maintaining aging facilities

Replace Old Mindsets With a Quality Mindset

Our team knows establishing quality mindsets is hard but achievable. Process improvements are at the core of our expertise. We have helped companies of all sizes, from around the world, lay the foundation for creating a quality culture, one building block at a time.

LESS

Reduce Drug Shortages

“Given the investments the industry makes in product quality and surety of supply, why do drug shortages continue to happen?” asks NSF’s John Johnson.

Drug shortages are hugely damaging to our industry, potentially life changing to our patients and a constant source of concern to front-line colleagues in supply chain and pharmacies/ health care providers.

Former FDA Commissioner Scott Gottlieb announced in July 2018 that a reduction in the severity and frequency of drug shortages has to be a major priority and FDA will seek ways of working with industry to prevent the risk of a stock-out and minimize the impact when the worst happens. FDA’s Drug Shortage Task Force now report to Congress every 12 months on the actions taken to prevent and mitigate drug shortages and some progress is being made; though underlying concerns of manufacturing issues remain a hot topic for FDA and other international regulatory bodies.

But why is an industry that sits on a bedrock of systemic and measured controls, sets high degrees of self and international regulation, and prides itself on its contribution to world health is so often blighted by being unable to supply the right drugs in the right quantities at the right quality to all parts of the world?

Data shows it is not down to enforced austerity or loss of financial performance. See **Table 1**.

Investment has increased in many sectors, yet we are seeing a marked increase in drug shortages, throughout EU, USA and the rest of the world. See **Table 2** (next page). Why is this happening?

Are there any clues in the EFPIA report?

- > R&D spend in India and China grew at 9% and 11% from 2013-2017 compared to 4% in EU and 7% in USA.
- > Emerging markets leading with new chemical or biological entities have increased 10-fold from 1998-2002 to 2013-2017.

European Federation of Pharmaceutical Industries and Associations (EFPIA) ‘The Pharmaceutical Industry in Figures – Key Data 2018’:

Measure (EU only) from 2010 to 2017	Progress	Increase or Decrease
Production values	From 199,400 to 258,000 million euros	29% increase
Revenue at ex-factory prices	From 153,685 to 207,000 million euros	35% increase
Employment	From 670,088 to 750,000 FTEs	12% increase

Table 1.

- > 66% of the retail price of the medicine reverts to the manufacturer. This covers new R&D costs, ongoing cost and infrastructure, cost of quality and production; yet how much is being invested in reducing the risk of drug shortages?

A shift in production to India and China took off more than 15 years ago and there is an emergence of greater R&D spend in this region too. Global supply chains over the same period have become hugely more complex and fragmented. These trends were predicated by the search for more economic and more flexible product supply chains, but has this shift caused a corresponding volatility in surety of supply? Has complexity and risk been baked into new, more economic supply chains, thus causing unpredictable hidden costs of stock-outs, recalls and regulatory action? This seems logical, yet it’s difficult to find scientific linkage that proves this beyond doubt.



by John Johnson, Vice President, Pharmaceutical Services, NSF International

UK Daily Telegraph 1 October 2019

A poll of 4,000 pharmacists identified that:

- > 84% had shortages of HRT drugs, 67% had shortages of contraceptives
- > 58% has shortages of anti-epileptic drugs
- > 20% had shortages of ant-psychotic drugs

A survey by The Pharmacists' Defence Association (PDA) in August 2019 suggested that around 21% of prescription drugs had suffered shortages in the previous three months. More than 90% of respondents felt the shortages had increased over the previous year.

FDA Report on Drug Shortages – Root Causes and Potential Solutions 2019

56% of US health care providers had changed patient care or delayed therapy in light of drug shortages in 2018.

Drug shortages, including those that arise during emergencies, have been a persistent problem despite public and private sector efforts to prevent and mitigate them. Analysis presented by FDA at the November 2018 public meeting showed that the number of ongoing drug shortages has recently been increasing after declining from a peak in 2011, and drug shortages have been lasting longer, in some cases, more than eight years.

Table 2.

By researching the causes of regulatory action (a common cause of product shortage due to enforced recalls or product suspensions), it is clear that some companies are really struggling to meet the internationally recognized cGMP expectations; in part due to culture, leadership and often a lack of financial commitment to the facilities and expertise needed to remain in perpetual GMP compliance. Accepting the pharma industry as a highly competitive industry, are we sacrificing surety of supply for the economies of a global supply chain? Though the balance of cost may appear attractive (despite the high size of regret in case of regulatory censure, recall and loss of reputation), are we serving the patients responsibly when accepting drug shortages as part of a competitive industry? Have recalls and supply interruptions become so common that they are now merely collateral damage which is soon tackled, paid for and forgotten? Where does the patient fit in?

NSF has a unique insight into the reasons for drug shortages, recall and regulatory censure as we are frequently tasked with supporting and guiding GMP remediation programs across the world, and from our research the key causes appear to be:

- > Lack of senior management commitment to cGMP compliance and an absence of proactive management to ensure compliance to new requirements
- > Turnover of staff in key positions destabilizing institutional learning
- > Lack of investment in legacy facilities in some locations, especially associated with the data integrity expectations of laboratory equipment and quality management systems, or the in-process controls and contamination strategies expected of modern production processes
- > A focus on cost and delivery that can crowd out the imperatives of operating a pharma quality system that must proactively identify, evaluate and mitigate risk
- > A lack of business continuity planning, quality risk management and deployment of continuous improvement

DO YOU RECOGNIZE ANY OF THESE IN YOUR ORGANIZATION?

So, this year, why not:

- > **Put a stop to risks that cause drug shortages?**
- > **Stop making excuses for poor practice** and using ICH Q9 as a way of defending the status quo?
- > **Stop postponing staff education programs** (the best time to improve staff performance is always today)?
- > **Stop the trend to engage with the cheapest vendors**, with superficial review of their quality performance and on-site risks?
- > **Stop the turnover of your best staff**, by engaging them in meaningful projects that make a tangible difference to the patient?
- > **Stop the institutional acceptance of reworking, reprocessing and reinspection?**

And in the process, let's stop the reasons for drug shortages at source!

Drug Shortages

A Personal Matter



Martin Lush talks with local pharmacist Rory Towler

Rory Towler is a pharmacist who, together with his wife Jo, runs our community pharmacy in Kirkbymoorside not far from our UK office. Filling over 1,000 prescriptions weekly, they are on the frontline of community health care. To some, “drug shortage” is just a headline, but to Rory and Jo, and pharmacists like them, it’s personal.

Martin: *How long have shortages been an issue?*

Rory: Shortages vary in magnitude and type, from the complete stock out to delays of weeks or months. We started noticing problems about 10 years ago, but shortages have dramatically worsened in the last five years. In any given week there may be 20 to 30 product items we struggle to get hold of. Some shortages resolve in a few weeks but it can be months before supplies are available. HRT shortages are a good example. In 2019, 30 to 40 product types were completely unavailable. We’ve also recently experienced extreme difficulty getting hold of adrenaline pens (used to treat anaphylaxis), naproxen (pain relief) and nifedipine (hypertension) to name but a few.

Martin: *So, what do you do?*

Rory: On average we make 20 to 30 phone calls every week to manufacturers and wholesale suppliers to try and source out-of-stock medicines. We’re rarely told why

there is a supply problem or given a reliable delivery date. This makes it impossible for us to plan and to provide the reassurance our patients need. On some occasions the manufacturer blames the wholesaler and vice versa. We are often left caught in the middle. When stock becomes available, we must be quick; it can sell out within minutes. When stock is unavailable for months, the impact, on already over-worked GPs, is considerable. Take nifedipine as an example; clinically its recommended patients are kept on the same generic brand. If unavailable, GPs may be forced to switch patients over to another brand or drug with potential clinical consequences.

Martin: *How can the pharma industry help you better?*

Rory: Three things come to mind.

Number one: Please remember we’re your customer and we’re just trying to do our job to the best of our ability. On many occasions the people we speak to (manufacturers and wholesalers) are ill informed and disengaged.

Number two: Please provide us with accurate and reliable information so we can plan ahead and provide reassurance to both patients and GPs.

Number three: Although it may be just a supply issue to you, it’s personal to the rest of us. The pharmacist, GP and most importantly – the patient.



NSF PINSIGHTS

Did you know the key cost in regulatory action is the effect of unplanned drug shortages? Our GMP remediation process is proven to get your product back on the market sooner.



By Hana Mekonnen,
Senior Vice
President, Biometrics,
Amarex Clinical
Research, LLC, an
NSF International
company



& Deborah Cole,
Marketing Associate,
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To learn more about
the Amarex team,
read the news item
on page 23

Understanding Adaptive Designs for Clinical Trials

What is Adaptive Design?

Adaptive design, as defined by the U.S. FDA, is “a clinical trial design that allows for prospectively planned modifications to one or more aspects of the design based on accumulating data from subjects in the trial.”¹ Adaptive design characteristics include modifying an ongoing clinical trial in accordance with predetermined rules, based on data from interim analyses. Adaptive design allows for greater flexibility in clinical trials with benefits of adaptive design trials, or adaptive clinical trials (ACTs), including increased efficiency, better ethical protections, greater generalizability/understanding of drug effects and higher approval from sponsors. Overall, adaptive designs make better use of resources when conducting clinical trials.



History and Current Application of Adaptive Designs

In December 2016, the United States Congress passed the 21st Century Cures Act to facilitate patient access to available treatments by bringing products to market faster. The act modified the U.S. FDA drug approval process and instructed the FDA to update its guidance on adaptive designs for clinical trials.

Although the 21st Century Cures Act refers to adaptive designs as novel methods that can enhance trial efficiency and lead to better research outcomes, and although some of these designs are new developments, adaptive

designs found their way into biostatistics literature in the 1960s and 1970s. Due to implementation and interpretation challenges, however, adaptive designs were rarely used and application to clinical trials did not occur until the 1990s². Even with some acceptance within the pharmaceutical and biotech industry, to date, randomized controlled trials (RCTs) remain the gold standard in clinical research, and challenges to ACTs have delayed their adoption despite their multitude of advantages.

Concerns Regarding Adaptive Designs

Concerns regarding adaptive designs in clinical trials that have hindered their use include inexperience, fears from stakeholders and regulatory bodies and practical limitations and challenges of some adaptive design types.³

- > **Inexperience:**
Inexperienced researchers do not understand the added complexities of adaptive designs. Knowing when or when not to adapt a trial, how to strategically plan for logistical challenges and how to conduct complicated interpretations are skills of the expert biostatistician, not the novice.
- > **Fears from stakeholders and regulators:**
Changing rules in an ongoing trial creates complications and uncertainty, which can be intimidating to stakeholders and regulators. Lack of familiarity with new methods leads to conservative decision making (e.g., choosing familiar RCTs over ACTs).
- > **Practical limitations/challenges:**
Practical limitations are possible and challenges do exist. Special analytical methods are required to avoid increased chances of erroneous conclusions and bias, and for some design types, methods are not available to account for these increases. Efficacy gains can cause losses in other areas of a trial. Designing an adaptive trial takes more time than designing a traditional RCT, which can delay study start timelines. By adding modifications, logistical challenges arise in order to ensure trial conduct and integrity are preserved. Results gained from adaptive trials can be too specific to generalize, or lead to interpretability challenges.

Addressing Adaptive Design Challenges

To address the challenges associated with adaptive designs, the FDA suggests considering the following four principles during the clinical trial design stage:

- > Control for the chance of erroneous conclusions by addressing possible Type I error probability inflation. Statistical theory can be utilized as well as simulations that evaluate the chance of erroneous conclusions.
- > Bias in estimating treatment effects should be evaluated and available methods for adjusting estimates should be applied to reduce or remove bias whenever possible. If methods are unavailable, appropriate cautions to interpretation should be noted.
- > Adaptive design trial details should be pre-specified prior to trial conduct, and documented in the study protocol. It is important that all adaptations be completely specified to ensure trial integrity, maintain safety, minimize access to comparative interim data and control for erroneous conclusions.
- > Trial conduct and integrity should be maintained by predicting, and setting up safeguards to prevent, possible trial conduct issues. Controlled access to information should be addressed in this plan.

Successful Clinical Trial Examples Using Adaptive Design

Adaptive design modifications can be applied across all phases of a clinical trial and to numerous aspects of the trial design, including but not limited to, dose, hypothesis, study endpoints, treatment arms and sample size. Amarex's biostatisticians have successfully designed and conducted many adaptive design clinical trials, and NSF's investment will allow Amarex to do even more adaptive trial work. The following examples highlight our expertise and experience, having applied adaptations leading to efficacious outcomes for study sponsors:

- > Six different adaptive clinical trials using sample size re-assessment for indications including diabetic foot ulcer (DFU), venous leg ulcer (VLU), hot flashes, schizophrenia, weight loss and pain management. Many of these products went on to obtain market approval.
- > An adaptive clinical trial with modification to treatment arms (i.e., dropping an arm), with market approval pending for treatment of benign prostatic hyperplasia.

Take-Home Message and Regulatory Considerations

- > Adaptive designs offer innovative solutions to the rigidity of classically fixed, randomized controlled trials. Troubleshooting through modifications during the ongoing clinical trial process leads to study results that are informative and efficient, with increased ethical protection to participants while maximizing utilization of resources.
- > Adaptive designs are complex, but challenges and complexities can be overcome with the help of experienced biostatisticians, consulting on the clinical trial from design through study completion.

Lastly, consider the role that regulatory bodies play in facilitating clinical trial product development. Agencies such as the FDA have indicated increasing interest in adaptive designs, and they are here to help you through this process. The FDA encourages sponsors to explore a number of design options, discussing considerations with the appropriate FDA review division. FDA notes its role will be more extensive on later phase adaptive clinical trials and minimal on early-phase exploratory trial designs. An FDA evaluation will be enhanced by thorough documentation of adaptive design plans and thorough documentation of study evaluations and reporting of trial results.

¹ U. S. Food and Drug Administration. Center for Drug Evaluation and Research. (2019). Adaptive Designs for Clinical Trials of Drugs and Biologics. Guidance for Industry. Retrieved from <https://www.fda.gov/media/78495/download>

² Bothwell, L. E., Avorn, J., Khan, N. F., & Kesselheim, A. S. (2018). Adaptive design clinical trials: a review of the literature and ClinicalTrials.gov. *BMJ open*, 8(2), e018320. doi:10.1136/bmjopen-2017-018320

³ Pallmann, P., Bedding, A. W., Choodari-Oskoei, B., Dimairo, M., Flight, L., Hampson, L. V., ... Jaki, T. (2018). Adaptive designs in clinical trials: why use them, and how to run and report them. *BMC medicine*, 16(1), 29. doi:10.1186/s12916-018-1017-7



Regulatory Update

Pharma EU & ICH Updates



by Pete Gough,
Vice President,
Pharmaceutical
Services, NSF
International

Pharma EU News

EMA Nitrosamine Impurities Guidance

In 2018, nitrosamine impurities, including N-nitrosodimethylamine (NDMA), were found in several blood pressure medicines known as sartans. This led to some product recalls and a regulatory review, which set strict new manufacturing requirements for these medicines. Subsequently, nitrosamine impurities have been detected in other products.

On 19 September 2019 the EMA published guidance that asks marketing authorisation holders for human medicines containing chemically synthesized active substances to review their medicines for the possible presence of nitrosamines and test all products at risk.

The steps companies should take are:

- > Evaluate possibility of nitrosamines being present in every concerned medicine **within 6 months (by end of March 2020)**
- > Prioritize evaluations to start with medicines more likely to be at risk of containing nitrosamines
- > Take into account findings from CHMP's review of sartans
- > Notify authorities of outcome of risk evaluations
- > Test products at risk of containing any nitrosamines



NSF PINSIGHTS

Did you know NSF have a leading expertise in the field of nitrosamine risk assessments for APIs and drug products?

- > Immediately report detection of nitrosamines to authorities
 - > Apply for necessary changes to marketing authorisations to address nitrosamine risk
 - > Complete all steps within three years
- Health Canada, Swissmedic, and the South Korean regulatory authority have all also written to marketing authorisation holders with similar requests for risk assessments and subsequent actions, with similar deadlines.

Implementation of the Clinical Trials Regulation

This continues to be held up waiting for the Clinical Trials Information System (CTIS) portal to go live. In an October 2019 update, the EMA Management Board did not give any indication as to when the system was likely to go live.

Implementation of Safety Features

The safety features element of the 2011 Falsified Medicines Directive went live on 9 February 2019 but by the end of the year there were still numerous, serious flaws in this system. Unresolved issues include:

- > Stakeholders still not registered with their NMVO
- > Stakeholders not having installed equipment
- > Lack of understanding of difference between verification and decommissioning
- > Error message rate still too high

Revision of EU GMP Annex 1 on Sterile Products

A revised version, following more than 6,000 comments on the December 2017 draft, was approved by the Inspector's Working Group in late September 2019. At the time of writing it was hoped that the final text would be issued mid-2020.

Brexit

Following the UK general election, we now know that the UK will formally leave the EU on 31 January 2020. However, there will be a transition period until the 31 December 2020, so in practice nothing changes before the end of 2020. During 2020 the UK and the EU will try to reach a comprehensive trade agreement on their relationship from 2021 onward. If an agreement cannot be reached by the end of 2020, there remains the possibility of a no-deal exit.

ICH News

At the ICH meeting in Singapore in November 2019, the Brazilian agency ANVISA was elected to the management committee.

The troubled ICH Q12 (Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management) finally achieved step 4 approval at the ICH meeting in Singapore.

This guide has been significantly delayed by the EU saying late in development that some sections were incompatible with EU law. These problems would now appear to be resolved but if implementation in the EU does require a change in the law it may take longer than usual.

ICH Q12 is intended to extend the use of QbD to established products and therefore supplements the existing QbD guidance for drug substances and drug products during product development, registration and launch (ICH Q8, Q9, Q10 and Q11).

An Implementation Working Group has been established to produce training materials for Q12 by November 2020, with a view to the implementation of the new guideline starting shortly after in 2021.

Pharma US News

Modernizing Postmarket Pharmacovigilance

As mandated by the 21st Century Cures Act, FDA announced a new draft document, Best Practices in Drug and Biological Product Postmarket Safety Surveillance for FDA Staff. This draft includes a high-level overview of tools, methods, signal detection and evaluation activities, using varied data sources. It describes a risk-based approach for signal detection and evaluation of safety that takes product

characteristics into account. This means that certain products are monitored more extensively, e.g. new molecular entities, original BLA and biosimilars, first-in-class approvals, products with complex manufacturing processes, etc.

Drug Shortages: Root Causes and Potential Solutions

FDA issued a report, Drug Shortages: Root Causes and Potential Solutions. The Task Force put in place to review drug shortages evaluated 163 drugs that went into shortage from 2013 to 2017. It found that shortages more likely affected relatively low-price and financially unattractive drugs, and were more likely to be sterile injectables. The report includes recommendations to more closely analyze information on shortages and contracting practices that may be driving them. It also supports developing a system to measure and rate a facility's quality management maturity. The rating would evaluate the robustness of a manufacturing facility's quality system and its ability to deliver high-quality products reliably and without disruption. FDA thinks this rating system could be used to inform purchasers, group purchasing organizations and consumers about the state of, and commitment to, the quality management of the manufacturing facility making the drugs they are buying.

Enhancing Oversight of Homeopathic Drugs

FDA updated its 2017 draft guidance, Drug Products Labeled as Homeopathic Guidance for FDA Staff and Industry, to provide better oversight of homeopathic drugs. The update details a risk-based enforcement policy prioritizing certain categories of homeopathic products that could pose a higher risk to public health, including products with particular ingredients and routes of administration, products for vulnerable populations and products with significant quality issues. FDA also announced the withdrawal of (CPG) 400.400, Conditions Under Which Homeopathic Drugs May be Marketed, as it considers the policy guide inconsistent with its risk-based approach and no longer reflective of current thinking.

Generics/Biosimilar Approvals 2019

FDA reported the fiscal year 2019 figures for generic drug approvals, showing a total of 1,171 generic drug approvals (935 full

Pharma US Updates



by Marinka Tellier, Director, Pharmaceutical Services, Regulatory Affairs, NSF International



EU Medical Devices Updates



by Robyn Meurant, Executive Director, Regulatory Team, IVDs and Medical Devices, NSF International

approvals and 236 tentative approvals), exceeding the all-time record of 971 for fiscal year 2018. In addition, it noted the approval of 125 applications for first generics of drugs and an upward trend in the numbers of complex generic drugs, which have seen less competition. Also, it was reported that nine biosimilars received approval during fiscal year 2019, bringing the total of approved biosimilars to 25.

New FDA Commissioner

On 17 December 2019 Dr. Stephen M. Hahn was sworn in as the 24th Commissioner of Food and Drug Administration. Dr. Hahn is an oncologist, scientist and health care leader who served as the chief medical executive at The University of Texas MD Anderson Cancer Center, prior to joining FDA.

EU Medical Devices News

MDR and IVDR

There are less than six months remaining until the new EU medical device regulation comes into effect. The implementation of this regulation has been on a rocky road, with major concerns over a lack of designated notified bodies, readiness of supporting mechanisms such as the databases underpinning many regulatory requirements and guidance. In amongst the gloom, a “corrigendum” (correction and addendum) for both Regulation (EU) 2017/745 on medical devices (MDR) and Regulation (EU) 2017/746 on in vitro diagnostic medical devices (IVDR) was published. The MDR version provides for a longer grace period for certain low-risk medical devices, given the lack of notified bodies. This change has been received positively by impacted manufacturers. None of the changes in the IVDR version have much impact on easing transition for IVD manufacturers.

Officially the launch of EUDAMED, the database portal for many of the operations of the new regulations, has been deferred two years. This will have a major impact on practical

implementation of the regulations, but extension of the MDR transition period was not simultaneously proposed.

The call for experts to serve on advisory panels for the MDR and IVDR was extended. The European system has complex and stringent rules to help control any potential for conflict of interest, but it also makes it difficult to find suitably qualified candidates.

News on Notified Bodies

More notified bodies have been designated, but is it too little too late for medical devices? Visit the European Commission website for up-to-date information on notified bodies.



Medical Device Coordination Group (MDCG) Guidance

More official guidance for the new regulations was issued in the last quarter of 2019, and we hope to see quite a few more early this year. The focus of the eight new documents was primarily medical devices, which is not surprising given that the transition period for full adoption of the MDR is May 2020. The clarity of the new guidance on qualification of software as a medical device has met with mixed opinions, and this will no doubt create further confusion in an area with a lot of gray.

What can we expect to see in the next few months? According to the MDCG plan, medical device manufacturers should benefit (again, in not a particularly timely way) from guidance on significant changes, equivalence, clinical evidence for legacy products and templates for postmarket clinical follow up activities. For IVD manufacturers, the long-awaited classification guidance should be finalized as well as guidance on performance evaluation. More information on the European medical device nomenclature should also be published.

Forthcoming Courses

Pharma Courses Planned From March to April 2020

Pharmaceutical Formulation and Processing – Part 2

March 9 – 13 | London, UK | Course Fee: £3,330 excl. VAT



ROYAL SOCIETY OF CHEMISTRY | APPROVED TRAINING

Responsible Person and Good Distribution Practice

(Cogent Gold Standard Approved Training)

March 10 – 12 | Watford, UK | Course Fee: £2,170 excl. VAT

Pharmaceutical GMP Audits and Self-Inspections

(A CQI and IRCA Certified Training GMP PQS Lead Auditor Course)

March 16 – 20 | Ann Arbor, USA | Course Fee: £3,130 excl. VAT

Pharmaceutical GMP

March 17 – 19 | Amsterdam, Netherlands | Course Fee: £2,170 excl. VAT

Pharmaceutical Legislation Update

March 17 | Manchester, UK | Course Fee: £830 excl. VAT

ROYAL SOCIETY OF CHEMISTRY | APPROVED TRAINING

Pharmaceutical Legislation Update

March 19 | Amsterdam, Netherlands | Course Fee: £830 excl. VAT

ROYAL SOCIETY OF CHEMISTRY | APPROVED TRAINING

Regulatory Affairs for QA: Marketing Authorisations

March 18 | Manchester, UK | Course Fee: £730 excl. VAT

Regulatory Affairs for QA: Variations

March 19 | Manchester, UK | Course Fee: £730 excl. VAT

Pharmaceutical GMP Audits and Self-Inspections

(A CQI and IRCA Certified Training GMP PQS Lead Auditor Course)

March 23 – 27 | Manchester, UK | Course Fee: £3,130 excl. VAT

Pharmaceutical Quality Systems

March 30 – April 2 | York, UK | Course Fee: £2,960 excl. VAT



ROYAL SOCIETY OF CHEMISTRY | APPROVED TRAINING

Free Seminar for Prospective QPs and Sponsors

March 31 | York, UK | Course Fee: Free

A-Z of Sterile Products Manufacture

March 30 – April 3 | Manchester, UK | Course Fee: £3,270 excl. VAT

ROYAL SOCIETY OF CHEMISTRY | APPROVED TRAINING

Pharmaceutical Microbiology

April 20 – 24 | Brighton, UK | Course Fee: £3,330 excl. VAT



ROYAL SOCIETY OF CHEMISTRY | APPROVED TRAINING

Quality Risk Management

April 28 | Watford, UK | Course Fee: £730 excl. VAT

For more information email pharmacourses@nsf.org,
visit www.nsf.org/info/pharma-training or the **NSF Pharma App**.

Try our
eLearning!

To complement our face-to-face training, we offer a number of cost-effective pharmaceutical and medical device eLearning modules that can be completed at a time and place to suit you. Visit our website to see our range of eLearning.



Course details are correct at the time of printing and are published in good faith. NSF reserves the right to make any changes which may become necessary.

NSF News...

NSF Raises £2,808 for Ryedale Carers Support

During 2019, NSF's health sciences team in the UK raised a grand total of £2,808 for local charity Ryedale Carers Support. Ryedale Carers Support is a local voluntary organization and registered charity that provides practical and emotional help for carers, the people they care for and older people living on their own.



Fundraising efforts included a cake stalls at the Kirkbymoorside weekly market, a street collection and a "yard sale."

HELP US DO MORE FOR CHARITY



Continuing the theme of doing more, 2020 is a big year for Martin Lush (our Global VP) who turns 60!

To celebrate, this veteran of seven Iron Man Triathlons and 20+ marathons has decided to do more exercise. He has come up with

a 6/60/600/6000 challenge: swim 6 miles, run 60, cycle 600 and, in the process, raise £6,000 for Ryedale Carers Support.

If you would like to contribute to Martin's fundraising efforts, please visit www.justgiving.com/crowdfunding/martin-lush. Any contribution is greatly appreciated. We will keep you up to date on his progress, including photos of him suffering, albeit for a great cause.

Innovation Workshop Finds What Is Driving the Future of Medical Devices

NSF PROSYSTEM GmbH celebrated its two-year anniversary as part of NSF with an innovation workshop that also launched the company's rebrand as NSF International. The workshop, held on October 1, 2019 in Hamburg, brought industry leaders together for a day of sessions on the ways in which technological and regulatory change will mold the future of the industry.



"For 75 years, NSF International has been protecting and improving human health. Likewise, since 1999, PROSYSTEM has been a thought leader in biomedical engineering. In our two years together, we've witnessed the medical device industry begin to shift its focus from repair to prevention. That shift is going to accelerate as tech giants seek – and create – opportunities in the health care marketplace and regulatory bodies adapt to the impact rapidly-developing technology will have on patient safety." said Oliver Christ.



NSF International Expands Health Sciences Services With Acquisition of Majority Interest in Amarex CRO

NSF International has acquired a majority interest in Amarex Clinical Research, LLC, a clinical stage contract research organization (CRO) headquartered in Germantown, Maryland. The transaction supports NSF's mission of protecting and improving human health through

expanded consulting services to the medical device and pharma/biotech industries. As part of NSF International's global health science consulting business, the highly-respected CRO will be known as Amarex Clinical Research, LLC, an NSF International company.

The transaction creates a single access point for medical device and pharma/biotech product developers seeking integrated, expert services throughout the entire product lifecycle.

Amarex brings clinical trial expertise to NSF's large base of training, quality and consulting clients. It will leverage NSF International's global infrastructure to expand its contract research capabilities and better serve clients with the design and execution of clinical trials and navigating the FDA, TFDA and EMA regulatory approval process.

Since 1998, Amarex Clinical Research has been helping biotech, medical device and pharmaceutical companies conduct scientifically sound clinical trials and navigate complex regulatory environments in a wide range of therapeutic indications including, but not limited to, oncology, central nervous system, wound healing, infectious disease, cardiovascular and urology.

GMP FOR BIOLOGICAL AND BIOTECHNOLOGY PRODUCTS COURSE RELOCATES TO IRELAND

We held our GMP for Biological and Biotechnology Products course for the first time at the National Institute for Bioprocessing Research & Training (NIBRT). John Johnson, course tutor, said there was "rigorous discussion and discourse from very bright and challenging delegates looking to make a difference in our industry."



The course will be held again on 14-17 July, 2020 – reserve your places early so you don't miss out. 2019 was a sell-out!



2019 ISPE Singapore Conference and Exhibition

NSF's Lynne Byers and Rachel Carmichael attended the ISPE Conference and Exhibition in Singapore in August.



Lynne Byers took part in the Women in Pharma Brainstorming Lunch & Talk, facilitating a table discussion exploring topics such as the challenges of working in a global organization and managing a work-life balance.

With over 1,000 participants from 25 countries, Singapore's long-running pharmaceutical manufacturing industry event offered focused and insightful learning opportunities and networking opportunities.

RESPONSIBLE PERSON *and* GOOD DISTRIBUTION PRACTICE TRAINING

An interview with Catherine Kay, NSF's Executive Director of Pharmaceutical Services

How long has NSF been providing GxP Training?

NSF has been providing instructor-led, interactive training programs for over 30 years and has been providing Good Distribution Practice training as a public course for the last two years. We are always keen to have our courses accredited by an independent organization and so applied to have our GDP course mapped against the Cogent Gold Standard.

What is the Cogent Gold Standard?

Cogent Skills (alongside the MHRA) have developed a new Gold Standard role profile for a Responsible Person in Medicinal Products. The standard sets an industry-agreed framework that identifies the skills required by a Responsible Person in four areas. This ensures that the role includes not only the traditional qualifications and technical requirements, but also behavioral skills required to do the job to a high standard. These include business improvement, leadership and communication. On completion of the course, all delegates complete an online assessment and following a pass result, receive a certificate from Cogent Skills featuring the MHRA logo.

What are the key challenges for the RP?

At the most recent MHRA GDP Symposium in November, Peter Brown, Senior Medicines Inspector at MHRA, shared the top five deficiencies from GDP inspections in 2018/19:

- > Quality Management, 28.5%
- > Transport, 21%
- > Documentation, 21%
- > Responsible Person, 15%
- > Risk Management, 13.5%

Quality systems are often not fit for purpose, especially when the company has expanded. The largest contributor of deficiencies in this area is that outsourced activities, such as transportation audits being completed within a two-year cycle, are not being controlled effectively.

Other areas of note are lack of visibility of transport routes and poor export controls, poor documentation, user traceability and missing C88s (single administrative document).

For the second year in a row, the lack of definition of the RP duties and uncontrolled delegation of duties has been a top five deficiency, along with a lack of oversight of commercial matters.

Other emerging trends are the poor understanding of the supply of medicines into territories where there is no license in place, cloned company credentials and falsified GDP certificates from another EU authority.

Overall, IAG (Inspectorate Action Group) and CMT (Compliance Management Team) case numbers are increasing significantly.



What is the RPi role?

If there is a no-deal Brexit, a wholesale dealer may import Qualified Person (QP) certified medicines from the European Economic Area (EEA) if certain checks are made by the Responsible Person (import) (RPi). The RPi is responsible for implementing a system to confirm that the required QP certification has taken place for products that have been imported into the UK from countries on a list (initially, countries in the EEA).

Is the training just for trainee RPs?

The training is extremely relevant to trainee RPs, but also provides refresher training for current RPs, as well as new warehouse supervisors and managers or personnel who are new to GDP operations, auditors who are expected to inspect storage facilities and personnel from new distribution operations.

Visit www.nsf.org/info/pharma-training for more information on the course and to see 2020 dates.



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