

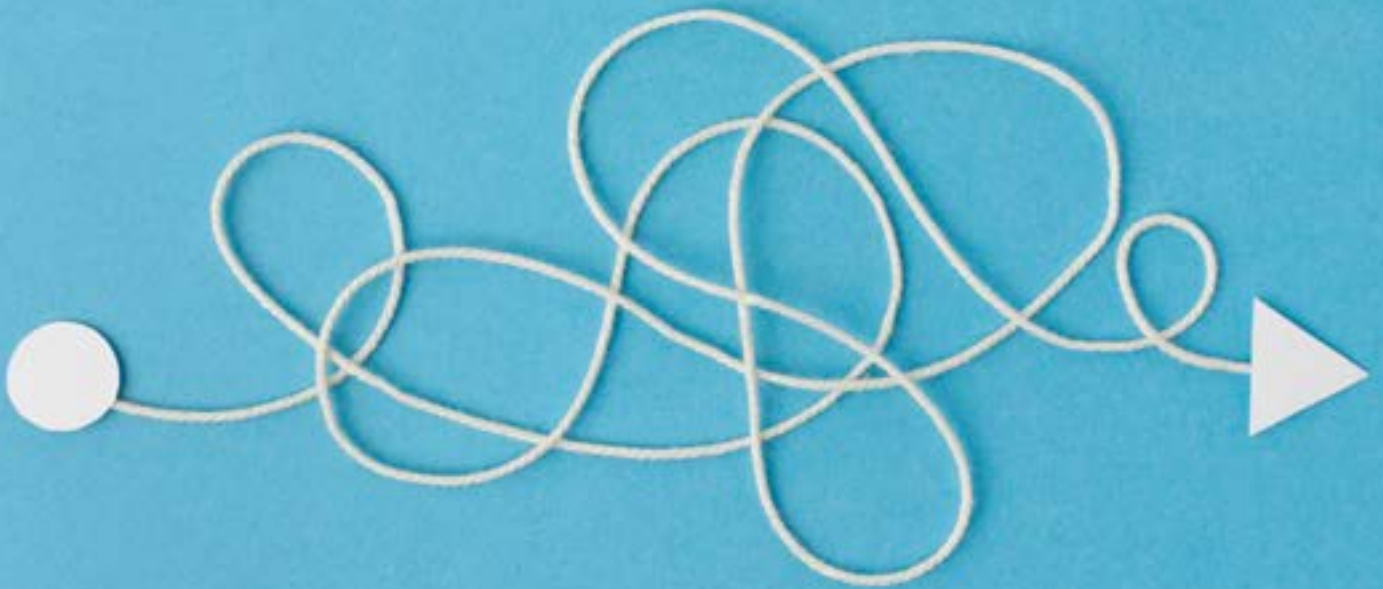
Journal

2017, Issue 39



Simplicity

CRITICAL FOR SUCCESS
IN YOUR QUALITY SYSTEM



www.nsf.org



welcome

I recently wrote an article on LinkedIn, **What Would Steve Jobs Tell the Pharma Industry?** It obviously struck a chord. Over 6,000 of your colleagues and industry peers have read it. Its general theme is that the pharmaceutical industry must reinvent itself, and quickly. This must start with brutal simplification of everything. Simplification is survival. Take a look at the excellent article on CAPA systems by Andy and Mehul on page 7. It provides invaluable advice on how to ensure your CAPA system is simple, robust and compliant. Jesse's case study on quality systems (page 10) shows what is possible and how one of our clients reduced its SOPs by 67 percent and the total number of forms by 88 percent!

Our mission at NSF is really simple. To make a positive difference to our clients and to have as much fun as possible doing it! Helping companies simplify their systems to improve efficiency and reduce risk is always rewarding, as is helping the wider community. Thanks to you we've been able fund research into nanoparticles for the treatment of kidney disease and in cancer therapy. We have also helped fund Ph.D. students in their research into pulmonary disease and novel drug delivery systems. Take a look at page 22 – our team members also walked 22 miles along our stunning (and hilly!) coastline to raise £500 for local charities.

So welcome to the 39th edition of the Journal. We hope it inspires you to simplify, make a positive contribution to your patient community and have as much fun as possible.



Martin Lush



Martin Lush,
Global Vice President, NSF Health
Sciences Pharma Biotech Consulting
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Audit

How to Write to Regulatory Agencies When Things Go Wrong

Your Essential Guidance



by Martin Lush,
Global Vice
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Devices

The Story So Far

It's Friday, it's late and you are just leaving for the weekend. The inspection you hosted two weeks ago remains a painful memory. The exit meeting didn't go well. There were five major observations all relating to your quality system. When your boss enters your office, you know it's not to wish you a good weekend. She looks stressed, anxious and keen to offload a big problem.

"We've received the regulator's audit report. We now have one critical and seven majors, and we have 15 days to respond in writing. Our license to operate is at risk. Please cancel your weekend. I need the draft response by Tuesday."

So What Do You Do?

Firstly, acknowledge receipt of the report immediately. Always be respectful and polite, never defensive or officious. Keep this immediate communication short and to the point. Commit to providing a full and comprehensive response within the permitted time frame. Emphasize your total commitment to fix the underlying causes and to address any immediate risks... and then leave for the weekend! This is not a frivolous point. So many responses are written by people who are tired, stressed and just not thinking straight.

When putting anything in writing, imagine you are the regulator.

In writing the audit report, the regulator is (subconsciously) expressing two emotions. Fear over patient safety and/or lack of trust and confidence in your company. Your primary objective is to reduce both fears and engage in a dialogue that seeks to rebuild credibility.

Fear: The auditor's primary objective is to safeguard public health. A damaging audit report means they have concerns about your company's ability to manufacture products that

are safe, efficacious and of the right quality. This may be due to specific observations or just a feeling that systems, procedures or practices are not in a state of control.

Lack of trust and confidence: Poor inspections quickly erode trust and confidence between the regulator and your company. The relationship between company and agency has been badly damaged. Remember, auditors are human! Although good auditors base conclusions on facts, emotions (gut feel) will play an important part in how they perceive your company, your leadership and your quality culture. This is not a precise process and cultural differences can often sabotage good intent. These cultural differences can easily lead to miscommunication and misunderstanding that then create the gut feeling of distrust.

Doing any of the following during an inspection will erode trust:

- > Not answering questions clearly
- > Not providing documents quickly or using delaying tactics in general
- > Attempting to justify bad practices using risk assessment

- > Appearing to hide bad data
- > Not being transparent
- > Putting barriers in front of the inspector (making their life tough!)
- > Management answering all of the questions

So, when responding to regulatory criticism, remember:

- > Your primary objective is to rebuild trust and remove fear. Don't just focus on providing data and information
- > Accept that rebuilding trust and removing fear takes time, often years. Be consistent and genuine in your messaging. Don't attempt to fake it
- > Even if you feel that you have been ill-treated or misunderstood, or the inspector was just having a bad day, remember the perception of the inspector is their reality, particularly when it's in writing! Companies who feel victimized or unfairly treated often respond emotionally, making the situation worse

Before writing to the regulators, remember the essentials:

- > Speed is of the essence. Make it clear which actions you will take immediately to protect patient safety. Be thorough in justifying why some products and markets are at risk and others are not
- > Don't just rely on words; phone calls and face-to-face meetings are always better
- > Choose your words carefully. If you were misunderstood once, it can happen again!
- > Less is more. Make sure your response is easy to understand and easy to navigate.

Regulators are busy people. Your response may be the center of your universe but it is not the same for them! A response that is simple to read and understand, and which conveys your desire to rebuild trust and respect by delivering what is needed, will be well received

- > Make sure your response is credible and that the resources and financial investment required will be made available. Fixing big problems without investment is not credible. Attempting to fix problems with the same thinking that created them will not be well received
- > Convey the support and active engagement of your senior leadership. Their involvement must be front and center stage. After all, they are ultimately responsible

Never ever:

- > Openly disagree with the auditor's findings
- > State that you've been audited by other regulatory agencies who gave you a clean bill of health
- > Respond only to single observations and ignore the big picture
- > Treat the symptoms, not the cause. If you find yourself including statements such as 'SOP rewritten,', or 'policy document updated' or 'retraining completed,' rip it up and start again
- > Justify bad practice by using risk assessment, validation or spurious statistical methods
- > Over promise and under deliver
- > Be anything other than truthful and sincere



Drafting Your Response: Down to the Specifics

Step 1: Mindset

- > Get rid of the victim mentality and mindset quickly
- > Focus on meeting the emotional needs of the regulator; rebuild trust and remove fear in actions, not just words

Step 2: Ask Yourself if the Observation is Factually Correct

Or has there been some misunderstanding or any miscommunication between you and the regulator? Always view this from the auditor's perspective. Acknowledge any potential misunderstanding by providing the real facts and data. Accept responsibility for not conveying these clearly during the inspection. Remember, the effectiveness of communication is measured by the response you get. If there has been any misunderstanding, it's your fault, not the inspector's.

Step 3: Acknowledge Each Observation

Accept the validity of all observations that you feel are justified. However, if you don't agree with the observation or criticism, you must say so. You must defend your position based on good science, good regulatory practice and common sense.

For example, one of our clients was cited for insufficient detail in an SOP covering gowning procedures. The auditor felt that the three-page SOP with eight photos and very few words was not detailed enough to ensure consistency of practice. The company rejected the validity of the observation by providing:

- > A copy of the comprehensive education program that supported the SOP
- > Gowning validation data demonstrating excellent consistency in practice
- > Exit monitoring data showing excellent levels of aseptic practice in the manufacturing area
- > The latest research on cognitive overload, emphasizing that pictures are better than words and that less is more for instructional details

They also provided the regulators with links to NSF webinars and resources:

- > The Art and Science of Simplification – How to Win Your War on Complexity
- > Human Error Prevention – Solutions and Answers

Visit www.nsf.org/info/pblibrary

Step 4: Complete a Far-Reaching Risk Assessment

This must address:

- > Potential severity of harm
- > Probability of occurrence
- > Likelihood of detection/non-detection

The scope of the risk assessment is vital. When did this issue first happen? How many batches are involved? Remember, these deficiencies probably extend to other plants in your network. Do not limit your risk assessment and CAPA plan to the plant in question or just to the specific observation.

Step 5: Identify Your Immediate Risk Mitigation (Correction)

What steps will you take immediately to mitigate risk? Who will do what, by when? What are your milestones and measures?

- > Stop manufacturing?
- > Quarantine product?
- > Recall product?
- > Replace equipment?

How will short-term corrective actions be monitored and measured for effectiveness? What resources will be dedicated to successful implementation?

Step 6: Identify the Error Chain

What caused this to happen? Why didn't you pick this up and fix it? This step is vital. A detailed review of all contributing factors (error chain) that led to the deficiency is essential. Take, for example, failure to set the correct specification for environmental monitoring.

The questions the regulatory agency want answered include:

- > Why did your own internal surveillance systems fail to pick this up?
 - Self-inspection program
 - QA (in general)
 - Corporate audit
 - Deviation and CAPA system
 - Plant reviews and more
- > Why did people throughout your organization fail to implement the correct standard?
 - Ignorance of poor GMP requirements
 - Poor training or education
 - Fear
 - Etc
- > Why did the quality system allow this to happen?
 - Why did policy documents and SOPs fail to include the right standard?

Step 7: Prevention

Preventive actions are key to rebuilding trust and respect. They communicate your commitment

to prevention and improvement rather than the quick fix. Who will do what, when and how? What are the timelines and milestones? How will effectiveness be monitored, measured and reported? Have you engineered out the primary causes. How have you addressed the cultural and behavioral issues?

Step 8: Your Cover Letter is Vital

The first thing the regulator will read is your cover letter. Usually written by you and signed by a member of your senior leadership team. The more serious the audit report, the more senior the signature. It must convey:

- > How serious you are about addressing the issues raised
- > The immediate actions you have taken to reduce risk to patient safety
- > Your commitment to fixing the underlying causes
- > The resources that will be mobilized to enable this to happen
- > Your willingness to work collaboratively with the agency

Responding to Severe Regulatory Criticism?

1. Think first. Let logic rule over emotion
2. Your focus is to satisfy the emotional needs of the regulator by removing fear and rebuilding trust and respect. It's about style and content
3. Correct any misunderstandings but never attempt to justify the unjustifiable
4. If you feel any criticism is not justified, respectfully defend your position using science, data and common sense
5. Make sure your response focuses on prevention, not short-term reaction, and that your plan is credible and fully resourced
6. Ensure your response is simple to understand, and easy to read and navigate. It must communicate your sincerity and commitment to address the underlying causes, not just in words but by the actions of leadership

If you need assistance or have questions, please contact us at pharmamail@nsf.org

Many of these same principles apply to medical device manufacturers when they receive FDA warning letters. Kristen Grumet, Executive Director at NSF International's medical device business published an article in the Medical Design and Outsourcing publication on six key steps manufacturers can take in response to a FDA Form 483 and Warning Letter. Please download a copy of this article by visiting www.nsf.org/info/formfda483md
For more information on NSF's medical device services visit www.nsfmedicaldevices.org

Do You Have a Robust and Compliant CAPA System?

Let's find out.

Pharma biotech companies around the globe are struggling to juggle numerous priorities and challenges. One of their biggest struggles is to effectively manage CAPAs.

1. Do you use a scored risk assessment process to determine the need for an investigation and CAPA?
2. Do fewer than 10 percent of your investigations conclude human error as the root cause?
3. Do you maintain and use metrics on how your CAPA system is performing?
4. Do you perform effectiveness checks that include objective and measurable criteria?
5. Do fewer than 25 percent of your CAPAs need extensions?

Unless you answered YES to all of the questions, your CAPA system may not be as robust and compliant as you think.

Symptoms of an Ineffective CAPA System

Pharma biotech companies that lack robust and compliant CAPA systems may be struggling with one or more of the following common problems:

- > Employees focus on closing the CAPA to release the batch rather than applying a systemic approach to resolve and remediate the problem and prevent it from happening again
- > CAPA actions address symptoms but do not fix the underlying root causes
- > There is a lack of expertise in developing, implementing and maintaining (and sometimes enhancing) a CAPA system that integrates compliance into business practices and quality systems
- > The CAPA system may be good but personnel do not use, or do not have the knowledge and expertise on to effectively use, the CAPA system to improve profitability by decreasing the cost of quality
- > The CAPA system doesn't use effective checks and thereby results in unintended consequences
- > The CAPA actions add unnecessary complexity and inevitably lead to non-compliance with local procedures

CAPA Advice

Not just for tracking

A CAPA system is not just a formal tracking system, it is the central component that encompasses all of the mechanisms and data sources that a sound quality system uses to monitor the quality of people, processes, product and problems. The CAPA system is an overarching umbrella – all control points flow through to the CAPA system.

Goldilocks and CAPAs

We have come across several companies that seem to be reluctant to open another CAPA for fear of overwhelming the system. This may result in under reporting of CAPAs which is a missed opportunity to fix problems and drive improvement. There is perception that having too many CAPAs is a bad thing and indicative of poor control over the pharmaceutical quality system. There is a fine line between having too many vs. not enough CAPAs, so one should strive towards a Goldilocks model – where you have the number of CAPAs that are just right. A facility must have appropriate mechanisms in place to determine when a situation merits issuance of a CAPA. It must be understood that not all investigations will result in a CAPA.



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One example may be an investigation in which the root cause has not yet been determined. Some companies in this situation will initiate a CAPA anyway, which is not value added. CAPAs initiated at this stage will divert resources to complete the action plans but will not reduce failure rate. Sometimes it is necessary to wait until there are several non-conformances before a pattern that points to the root cause can be identified.

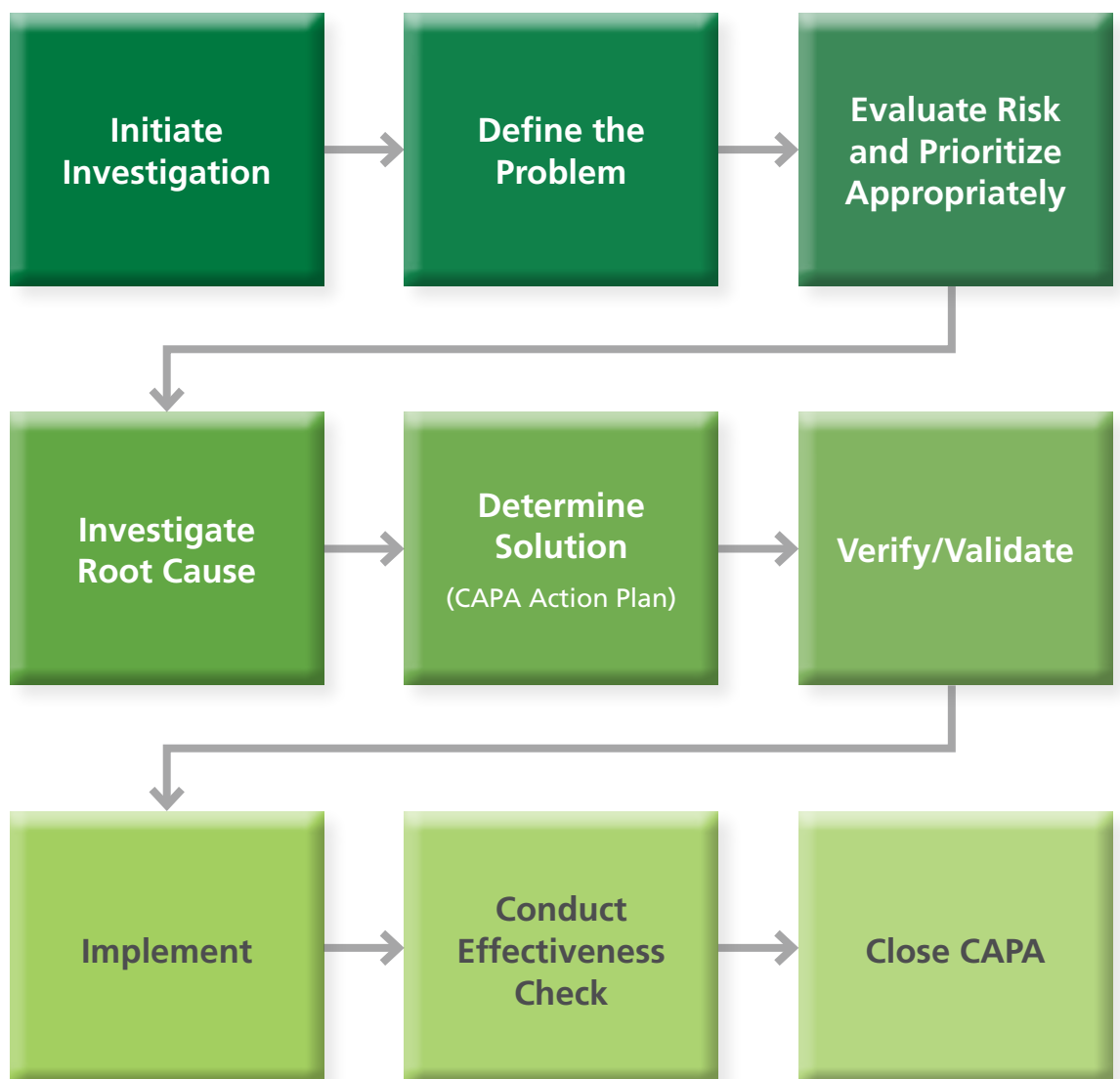
How long is too long?

Once the root cause is identified, evaluate the CAPA. Some CAPAs will be quick and easy to implement whereas the others may have long lead times, e.g. equipment redesign. If the CAPA will remain open for a longer period of time, the CAPA system should track the status and document the milestones. It is not good practice to leave a CAPA open long with no indication of activity. Time flies

and at times a CAPA deadline is missed. The first solution to this problem is to set realistic timelines for completion; too many of us are overly optimistic about the time needed to implement improvements. However, when it becomes clear that the deadline will not be met, it is a good idea to include a system for CAPA extensions. It is recommended that you have an escalating level of approvals for extensions – for example, the first extension requires department approval while the last extension may require executive level approval. The system should have the ability to capture status information and milestones as well as rationale for the extension and the risk of not closing as per the original date.

CAPA Essentials

The CAPA process can be simplified as below:





Pharma biotech companies can improve their CAPA processes by:

- > Implementing a CAPA system that is simple, easy to follow, risk-based and easily integrated throughout the organization
- > Implementing a standard set of root cause analysis tools
- > Using data analysis tools and processes within the CAPA system
- > Configuring data so similar problems can be categorized to facilitate trending and further data analysis
- > Determining the frequency of data analysis and metric review
- > Identifying adverse trends in real time and intervening before they deteriorate into non-conformances

During the course of CAPA process, if you discover a new piece of information or come across a new learning, evaluate and communicate it. Also ensure that it cascades through and eventually gets implemented to other products, quality systems, and across the organization as appropriate.

Death by CAPA (Overkill Effect)

While trying to develop or enhance a robust and compliant CAPA system, companies sometimes overdo things and end up adding unnecessary elements in their CAPA system. These elements start strangling the company and thereby cause the death by CAPA effect.

Companies need to be very careful as they can easily fall into this overkill trap. They can suffer death by CAPA by having either too many CAPAs or an overly complicated system. An effective system requires a balanced approach. You do not want to develop a CAPA program that ends up requiring a CAPA!

To avoid death by CAPA:

- > Use a risk-based filter and prioritize events according to size, scope and severity
- > If possible develop and use a scoring system
- > Adequately train qualified personnel
- > Get advice from experts

Need Help?

NSF has a proven track record of helping companies mitigate and remediate such situations. In-house experts at NSF can help you and your company:

- > Assess gaps in your current CAPA system and help determine if it is robust and compliant
- > Address gaps and help to improve your existing CAPA system
- > Effectively train your staff on a new CAPA system
- > Provide coaching and mentoring on CAPA management
- > Assess and avoid death by CAPA situations

For further resources on this subject, visit our resource library www.nsf.org/info/pblibrary

White Paper: Your CAPA Effectiveness Ladder

Webinar: Improving CAPA Effectiveness to Drive Down Repeat Incidents

White Paper: Deviation and CAPA Systems

Quality System Case Study



by Jesse Ahrendt,
Executive Director
NSF Health Sciences
Pharma Biotech
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NSF recently worked with a U.S. based client's site in India, which involved consulting in three categories:

- > Remediation of quality systems
- > Data integrity improvements
- > Training and education of subject matter experts (SMEs)

This pharmaceutical quality system (PQS) improvement project had three main objectives.

Situation	Objective	
<p>Full re-deployment of the PQS which required an assessment and further enhancement of all SOPs associated with the PQS.</p>	<p>The PQS re-deployment project involved the assessment of approximately 550 local and corporate SOPs (as well as approximately 900 forms), which were reviewed and evaluated by NSF for compliance with corporate governing procedures and policies, as well as with cGMP regulatory expectations. The client expectations required further enhancement that resulted in a new governing body of procedures.</p>	
<p>Re-deployment of all newly enhanced procedures requiring creation and delivery of specific training and education modules across the site.</p>	<p>The training and education expectation was that all newly created procedures would be deployed to site personnel with classroom instruction. This includes requirements for comprehension and associated testing with the expectation that personnel must meet the grading requirements prior to being allowed to perform the tasks. NSF developed and conducted this training to all client-identified personnel in a phased approach.</p>	
<p>Implementation of interim controls for general documentation, as well as specific data gathering activity across the site to mitigate prior data integrity issues and prevent further issues, while educating personnel and developing processes to prevent further recurrence.</p>	<p>NSF developed and implemented the data integrity program and the interim controls that allowed employees to be trained on the importance of data integrity, and also created strict allowances for documentation and concurrent review of those activities. This was needed to allow further work to be conducted on the site.</p>	



Approach/Methodology	Returns on Investment & Outcomes to the Client
<p>The PQS in place was divided into appropriate subsystems (e.g. training, management responsibility, materials control and environmental monitoring). Each subsystem was assigned to an SME consultant who assessed all related SOPs that were in place (both local and corporate). Enhancement of those existing SOPs was then completed by NSF, either through revision or complete re-creation of the procedures. The enhancement process also included discussion and agreement with the SMEs from the site group.</p>	<p>Highlights:</p> <ul style="list-style-type: none"> > 67 percent reduction in the total number of SOPs (from about 550 down to 180) > 88 percent reduction in the total number of forms (from about 900 down to 100) > Creation of about 175 new training presentations that were given to the impacted personnel across 124 training sessions <p>The client was left with an entirely new operating system in regard to the PQS that should allow them to operate (re-start) their facility at a higher level of regulatory compliance than was previously possible. The reduced number of SOPs and forms allowed a major simplification of their previously overburdened and overly complicated systems.</p> <p>Because site SMEs were involved in the discussions, they will now be able to build on this new group of documents and the process overall to continue the efforts and expand into other key areas that may require this kind of enhancement exercise in the future. Our input provided the groundwork for the client to be able to re-start its manufacturing block.</p> <p>After NSF delivered training at the site, the QA group understands what a more detailed level of training looks like and will be able to continue this kind of delivery into the other areas that may be assessed in the future.</p> <p>The site is much more aware of what is required for data integrity, how to achieve it as a site goal and what some of the pitfalls are in relation to data and documentation management. They have also put controls in place that allow data to be trusted at a higher level than previously possible. This process created a shift in culture and exhibited behaviors throughout the entire organization.</p>
<p>The training program was assigned to two NSF individuals who created the training materials for presentation and delivered the requisite training. Training was largely provided in the local language. These materials consisted of a PowerPoint presentation as well as a written assessment for each training module created.</p>	
<p>Data integrity was approached through the establishment of two distinct protocols. The first protocol provided very strict controls to assess personnel behavior and to assure that personnel had a comprehensive understanding of the requirements. The second protocol was initiated once confidence was gained and it was assessed that the controls from the first protocol had been engrained into the daily processing work of the site personnel. It removed some of the more strict requirements that were in place, while still leaving controls that would continue to build confidence that the personnel were adapting to the new environment for cGMP documentation requirements.</p>	



by Jim Morris,
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Tech Talk



ADVANTAGES OF EXCIPIENT GMP CERTIFICATION

Making a case for GMP certification of an excipient manufacturer should be a straightforward exercise since the benefits appear so clear cut and regulatory guidance in the EU underscores the value of certification. Specifically, Chapter 3 of the EMA Guidance on formalized risk assessments to determine the appropriate GMP for a pharmaceutical excipient states that “certification of quality systems and/or GMP by the excipient manufacturer and the standards against which these have been granted should be considered as such certification may fulfil the requirements”. Furthermore, FDA participation in the development of a consensus standard, NSF/IPEC/ANSI 363 Good Manufacturing Practices (GMP) for Pharmaceutical Excipients, reinforces agency interest in ensuring pharmaceutical excipients are manufactured to an appropriate GMP standard. This article summarizes the benefits of an excipient GMP certification program (ECP) both from the point of view of the excipient manufacturer and the excipient customer.

Benefits to the Excipient Manufacturer

As an excipient certification body, one of the primary benefits is significantly improved quality systems and quality compliance at the excipient manufacturer. We have seen these improvements in the months leading up to GMP certification and continuing during the years immediately following GMP certification. Some excipient manufacturers were already at a high level of GMP compliance, and GMP certification provided confirmation of the maturity of their quality program. Other manufacturers needed to make significant improvements to their quality systems and, in some cases, their facilities in order to meet the requirements of the NSF/IPEC/ANSI 363 standard.

Yet, both groups of companies have realized the benefit of increased operator risk awareness, more effective internal audits, greater process understanding, increased cross-functional communication, and clear evidence of management’s commitment to quality management principles. These benefits are often difficult to monetize however a single problem avoided through increased operator GMP awareness can result in significant cost avoidance.

Benefits to the Excipient Customer

Excipient customers will typically modify their oversight of excipient manufacturers that have been GMP certified. They may move the excipient manufacturer further down on their supplier risk profile and choose to audit less frequently, if at all. Excipient customers are aware that in order to be certified, the excipient manufacturer must have systems in place and provide evidence that non-conformances and changes that require customer notification are handled appropriately. This assurance is typically not obtained through a one-day supplier audit that pharma companies carry out; rather, it is obtained as a result of thorough, multiple day audits of an excipient manufacturer as part of a certification audit program.

The benefit of an ECP for the excipient customer should be close to zero surprises and very low regulatory risk. Furthermore, excipients received from GMP certified manufacturers are excellent candidates for a reduced QC testing program.

Pharmaceutical excipient customers, particularly biopharmaceutical customers, are increasingly requesting more technical information to justify their selection of excipients. Therefore, it would be of far more value for the excipient customer to focus on the technical aspects of the excipient it is purchasing and worry less about GMP compliance once the excipient manufacturer is GMP certified. That is where the true value lies for both parties and ultimately for the end user or patient.

Consider the above benefits and select a certification scheme – such as NSF’s ECP – which will deliver long-term GMP improvement at your company, embed a culture of quality, and help your company establish a high level of confidence and trust with your excipient customers. If you are an excipient customer, select a GMP certified excipient manufacturer and reduce supply chain risk while freeing up resources to devote to other areas of the business.

Jim Morris has over 20 years of experience in pharmaceutical biotech consulting, including excipient GMP certification. For more information, please contact uspharma@nsf.org or call +1 202 822 1850

5 STEPS TO EXCIPIENT GMP CONFORMANCE

NSF/IPEC/ANSI 363



ARE YOU WONDERING HOW TO REDUCE COSTS AND IMPROVE SUPPLIER QUALITY AT YOUR COMPANY?

- > Did you know that NSF’s ECP can substitute for an on-site excipient supplier audit?
- > Did you know that NSF’s ECP is accredited by ANSI (ANSI-Accredited Product Certification Body – Accreditation #1180) and follows the ISO 9001 framework?
- > Did you know that excipient supplier audit reports can be obtained through the NSF ECP for a modest fee?

Focus your time and effort on things that really matter.

For more information, please contact uspharma@nsf.org/pharmamail@nsf.org or call +1 202 822 1850/+44 (0) 1751 432 999

New Toolkit for Improving Pharma Quality Systems



by John Johnson,
Vice President,
NSF Health Sciences
Pharma Biotech
Consulting

However you find out, and from whoever, the moment when you realize that your pharma quality system needs an overhaul is not a happy time. Dysfunctional quality systems always become apparent at the worst possible times and will consume attention, cost and time.

So when this happens, how do you choose the subjects that require overwhelming force if they are to be radically and permanently improved for the better?

ICH Q9 Quality Risk Management is useful when assigning finite resources to areas of major concern; it contains tools to assess the severity or consequences of doing nothing (the S), the occurrence or frequency by which the issue will manifest itself (the O) and the ease or detectability in case of an issue (the D). From the simple $S \times O \times D$ equation, it becomes clear what issues must be dealt with first; spinning off a site risk register, site quality plan and corresponding annual quality objectives.

Your success will depend on the engagement, commitment and competence of your wider team; and that will depend on the values and behaviors your company holds dear and also how you have invested in your team, both in terms of headcount and education levels. But how can you add structure and milestones to your improvement project and ensure that you invest in the expertise of the team at the same time?

The answer is BITE by BITE, step by step using NSF's Business Improvement Through Education approach.

BITE TOOLKIT

How does my PQS compare to cGMP expectations?

- > GMP and pharma quality system scorecard
- > GMP and pharma quality system facilitated assessment process

How can I assure our behaviors drive company performance for the long-term?

- > Behaviors driven by $B = M \times A \times T \times H$ (motivations, ability, triggers and habits)
- > Making change EAST (easy, attractive, social and timely)

How should I manage my next inspection?

- > Inspection preparation techniques
- > Inspection management techniques
- > Inspection remediation and follow-up
- > CAPA effectiveness checks
- > Management review tools and behaviors



How do I install staff education, not just training?

- > Training map and gap analysis toolkit
- > Custom training programs
- > Education across the science, compliance and leadership expectations of cGMP

How can I reduce complexity and set clear, unambiguous standards?

- > Cost of quality program
- > Human error reduction program
- > Value stream mapping
- > Simplification of communications and instructions including 'five to thrive'

How do I set standards for education and delivery?

- > Organizational development
- > Certification programs for company auditors
- > Certification programs for company deviation investigators
- > Certification of key roles, e.g. QC staff, steriles experts

To find out how to apply these tools, contact John Johnson or Rachel Carmichael at johnjohnson@nsf.org or rcarmichael@nsf.org

Learn how to tackle your demons BITE by BITE using our toolkit. For more information view our brochure at www.nsf.org/info/bitetoolkit

Regulatory Update

EU News

Clinical Trial Regulation Implementation

In December 2015 the EMA expected the EU Clinical Trial Regulation 536/2014 to come into effect by October 2018. However, in June 2017 the EMA pushed the implementation date to 2019 without specifying a month. This delay is due to technical problems with building the access portal that is essential to the new regulation.

Revised Medical Devices Legislation

On April 5, 2017 the European Parliament and Council approved two new regulations relating to medical devices: The Medical Devices Regulation 2017/745 and the In-Vitro Diagnostic Medical Devices Regulation 2017/746. These new regulations, published in the Official Journal of the EU on May 5, 2017, repeal the former Medical Devices Directives 90/385/EEC, 93/42/EEC, 98/79/EC and Commission Decision 2010/227/EU.

The Medical Devices Regulation 2017/745 has a three-year implementation period and the IVD Regulation 2017/746 has a five-year implementation period, both starting on May 26, 2017. Numerous other milestone dates for various provisions of these regulations will come into force after the initial implementation dates.

Safety Features Implementation

The European Commission has updated its Q&A on Safety Features to version 7. This guidance includes several updates as well as new guidance on technical specifications of the unique identifier (UI), verification of the safety features and decommissioning of the UI by wholesalers, and establishment, management and accessibility of the repositories system.

ICH News

New ICH Member and Observer

At the ICH meeting in Montreal, Canada on May 27 to June 1, 2017 the ICH Assembly admitted the China Food and Drug Administration (CFDA) as a member of ICH and the Pharmaceutical Inspection Cooperation Scheme (PIC/S) as an observer.

Brexit

New Location for the EMA

The EMA will have to relocate from London due to the UK leaving the EU. The European Commission accepted bids through July 2017 to be the EMA's new host city.

The draft relocation criteria stress that business continuity is vital and that the EMA needs to be operational in its new country by the time of Brexit (March 29, 2019) so that it can "maintain and attract highly qualified staff".

A decision on the new host city is expected to be made in November 2017.

EMA/EC Guidance on the Impact of Brexit

In May 2017 the EMA and EC published two guidance documents to help pharmaceutical companies responsible for both human and veterinary medicines to prepare for the UK's withdrawal from the European Union (Brexit).

In early May the EC published the document "Notice to marketing authorisation holders of centrally authorised medicinal products for human and veterinary use" which reminds companies that from midnight on March 30, 2019 the UK will leave the EU and become a 'third country.' The notice continues as follows:

"In this regard, marketing authorisation holders of centrally authorised medicinal products for human and veterinary use are reminded of certain legal repercussions, which need to be considered:

- > EU law requires that marketing authorisation holders are established in the EU (or EEA)



by Pete Gough,
Executive Director,
NSF Health Sciences
Pharma Biotech
Consulting



by Andrew Papas,
Vice President of
Regulatory Affairs,
NSF Health Sciences
Pharma Biotech
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Regulatory Update

- > Some activities must be performed in the EU (or EEA), related for example to pharmacovigilance, batch release, etc"

Preparing for the withdrawal is not just a matter for European and national administrations, but also for private parties. Marketing authorization holders may be required to adapt processes and to consider changes to the terms of the marketing authorization to ensure its continuous validity and exploitation once the UK has left the Union.

Marketing authorization holders will need to act sufficiently in advance to avoid any impact on the continuous supply of medicines for human and veterinary use within the EU.

In particular, the Commission and the EMA expect marketing authorization holders to prepare and proactively screen authorizations they hold for the need for any changes. The necessary transfer or variation requests will need to be submitted in due time considering the procedural timelines foreseen in the regulatory framework.

The second document, published in late May, is a question and answer document and is the first in a series of guidance documents.

The Q&A covers questions regarding:

- > The location of EU marketing authorization holders
- > Pharmacovigilance; location of the QPPV and pharmacovigilance system master file
- > Location of manufacturing and site of QP certification
- > The need for APIs exported from the UK into the EU to have written confirmation of GMP compliance from the MHRA unless the UK is added to the Commission's 'white list' of acceptable countries

The Q&A makes it clear that many of these operations that are currently being performed in the UK will have to be relocated to sites within the EU once the UK leaves.

U.S. News

New Commissioner of the Food and Drug Administration



Dr. Scott Gottlieb was sworn in as the 23rd Commissioner of the Food and Drug Administration on May 11, 2017. Dr. Gottlieb is a physician, Hodgkin's lymphoma cancer survivor, medical policy expert and public health advocate. He previously served as the FDA's deputy commissioner for medical and scientific affairs and as a senior advisor to the FDA commissioner.

He has indicated that his highest initial priority is to take immediate steps to reduce the scope of the current opioid addiction epidemic, including investigating opioid formulations designed to deter abuse.

Dr. Gottlieb also intends to tackle high drug prices and thinks the agency can have an influence by:

- > Preventing the industry from gaming regulations to get more exclusivity time without competition beyond what congress intended
- > Making it more straightforward for complex generic drugs to get to market (e.g. complex drugs like the EpiPen® or inhalers that competitors have a hard time getting approved)
- > Moving faster through the backlog of generic drug applications with approximately 4,200 ANDA applications pending approval at present, about half of which are pending industry's response to review questions

FDA Begins ORA Reorganization

After nearly four years of discussion and planning, the FDA has started its reorganizations of its inspection staff and expects it will take several years to be fully operational.

The Office of Regulatory Affairs (ORA)'s geography-based structure of five regions for inspectors and field laboratories is being replaced with a program-based structure in six areas: biological products, bioresearch monitoring, human and animal food, medical device and radiological health, pharmaceutical



quality and tobacco. ORA will still maintain its 20 district offices but they will no longer be organized within larger regions. District directors will keep their responsibilities, but will also specialize in one program as division directors.

Currently, perceived disparities from one inspection – or investigator – to another may be attributable to an investigator's inexperience or obligations to inspect multiple commodities. The ORA realignment effort is intended to reduce those inconsistencies.

Attention on FDA's oversight has increased as companies produce more complex drugs and devices, and challenges in food safety continue to mount. However, the FDA at present has no plans to close offices or relocate personnel. ORA has about 4,800 personnel, including approximately 1,600 investigators.

Also, the agency doesn't plan any reductions in employee numbers related to the new structure, as per Melinda Plaisier, associate commissioner for regulatory affairs, who oversees the staff under the ORA at the FDA.

eCTD Submissions to FDA

Under the Food and Drug Administration Safety and Innovation Act, FDA requires that certain submissions under the FD&C Act and the Public Health Service Act be submitted in electronic format, beginning no later than 24 months after issuance of a final version of a guidance document specifying the format for such electronic submissions. The final version of that guidance was published on May 5, 2015, thereby requiring all new NDAs, ANDAs and BLAs or supplements to existing NDAs, ANDAs and BLAs to be submitted electronically to FDA in eCTD format. New INDs have another year with a deadline of May 5, 2018.

For new drug master files (DMFs) or supplements to an existing DMF, FDA recognized the industry's challenges in meeting the May 5, 2017 date and has extended the eCTD deadline to May 5, 2018.

FDA Releases Draft Guidance for Comment on New ANDA Priority Reviews

FDA has distributed a draft guidance for comments, *ANDAs: Pre-Submission Facility*

Correspondence Associated with Priority Submissions Guidance for Industry, approximately 90 days before the new fiscal year begins in 2017 and before GDUFA II is approved. The agency is presumably taking this step so it will be ready for priority ANDAs early in the new fiscal year.

Under the draft guidance, priority ANDAs and priority prior approval supplements have expedited review timelines (8 months vs. 10 months for a priority ANDA, and 4 months (no pre-approval inspection)/8 months vs. 6 (no pre-approval inspection)/10 months for a priority ANDA PAS). These formalized priority review times were discussed and agreed upon during meetings held with industry and the public in hearings for GDUFA II.

FDA has had a prioritization scheme that moves certain ANDAs forward in an expedited review but it was never clear how much it may be expedited. Under the current draft guidance there are performance goals tied to these priority (and expedited) reviews if the applicant submits a complete and accurate pre-submission facility correspondence (PFC) no sooner than two months but no later than three months ahead of the ANDA submission. This PFC should contain the reason it should be considered for expedited review and detailed facility and study information for all of the GMP/BIMO facilities involved in the submission (API and FDP manufacturers, testing facilities, BE study facility, BE bioanalytical lab, combination product manufacturing site, etc.) This allows FDA to review the inspection history ahead of the ANDA and schedule any needed inspections earlier in the review cycle. One thing applicants should be aware of is that all facilities should be ready for an inspection at the time of the PFC submission and not at time of the ANDA/ANDA PAS filing.

FDA Publishes List of Off-Patent, Off-Exclusivity Drugs Without an Approved Generic

To improve transparency and encourage the development and submission of ANDAs in markets with no competition, FDA is publishing a list of approved NDA drug

Regulatory Update

products which are off-patent and off-exclusivity and for which the FDA has not approved an ANDA referencing that NDA drug product.

There are two parts to the list. Part I identifies drug products (identified by the API) for which FDA could immediately accept an ANDA without prior discussion. Part II identifies drug products involving potential legal, regulatory or scientific issues that should be addressed with the agency prior to submission of an ANDA or a 505(b) (2) NDA. For example, some drug products covered under Part II have no applicable product-specific guidance or are complex mixtures or imaging agents, or there are other regulatory complexities that may be overcome with additional information exchange between FDA and a prospective ANDA sponsor.

There are also some proteins identified in the list that may be reclassified as a biologic by 2020 as legislated in the Biologics Price Competition and Innovation Act of 2009. As such, they would not be eligible for an ANDA generic pathway but would require a biosimilar approval pathway.

FDA Published Draft Questions and Answers Guidance in Use of Electronic Records and Electronic Signatures in Clinical Investigations

This FDA guidance clarifies, updates and expands upon recommendations in the guidance for industry *Part 11, Electronic Records; Electronic Signatures – Scope and Application*. It provides guidance to sponsors, clinical investigators, institutional review boards, contract research organizations and other interested parties on the use of electronic records and electronic signatures under current regulations in clinical investigations of medical products.

This Q&A guidance provides explanations and suggested procedures to help ensure that electronic records and electronic signatures meet FDA requirements and are considered trustworthy, reliable and generally equivalent to paper records and handwritten signatures on paper. In addition, it provides guidance on the use of a risk-based approach when deciding to validate electronic systems, implementation of audit trails for electronic records and archiving

of records pertinent to clinical investigations conducted under parts 312 and 812.

One of FDA's goals in issuing this guidance was to encourage and facilitate the use of electronic records and systems to improve the quality and efficiency of clinical investigations.

FDA Announces Delay in Enforcing Serialization Requirements

On June 30, 2017, FDA issued a draft guidance for industry, *Product Identifier Requirements Under the Drug Supply Chain Security Act – Compliance Policy*. This guidance informs manufacturers and other supply chain stakeholders that although manufacturers are required by the Drug Supply Chain Security Act (DSCSA) to begin including a product identifier on prescription drug packages and cases on November 27, 2017, the FDA is delaying enforcement of those requirements until November 2018 to provide manufacturers additional time and avoid supply disruptions.

The compliance policy outlined in the draft guidance applies solely to products without a product identifier that are introduced into commerce by a manufacturer between November 27, 2017 and November 26, 2018.

While manufacturers work to meet product identifier requirements, they must comply with other DSCSA requirements.

Have a question on any of the updates?

Stay in touch through our new pharma app. With our **Ask an Expert** feature, in one click, you can ask a question to one of our many NSF industry experts and receive a response within 48 hours



NSF News...



NSF staff recently participated in two industry events...

2nd PDA Europe Annual Meeting

At the 2nd PDA Europe Annual Meeting on June 13-14, 2017 in Berlin, Martin Lush, Global Vice President of NSF Health Sciences, opened the proceedings with the presentation, The Political Landscape and the Future of the Pharmaceutical Industry.

Martin contacted over 700 industry experts for views and opinions. Key points of the talk include:

- > Even though our industry is renowned for changing slowly, the rate of change we will experience in the next 10 years will exceed the previous 40!
- > As an industry we must rebuild trust, invest in education and modernize outdated laws and regulations currently suffocating innovation and putting patients at risk
- > Without collaboration with regulators, payers, investors, innovators and (most importantly) PATIENTS, we will not be able to meet the healthcare needs of the next generation
- > Our industry must become risk wise and not risk averse
- > We have to shape the future, not plan for it

Contact Martin at martinlush@nsf.org to receive a copy of his presentation.



Making Pharmaceuticals

The NSF team was happy to meet many new and existing clients at Making Pharmaceuticals at the Ricoh Arena in Coventry, England on April 25-26. The busy event covered the detailed and complex issues associated with sourcing, manufacturing, outsourcing and delivering consistent pharmaceutical products to the market.

We asked clients who visited our stand three key questions regarding GMP deficiencies and gave them the opportunity to contribute answers so that we could feel their pain points and get their opinions on what the pharma industry should be doing to overcome these challenges. After the event, John Johnson, Vice President, NSF Health Sciences Pharma Biotech Consulting put together an article using the feedback as well as links to further resources that will help you going forward.

Both Pete Gough, Executive Director, NSF Health Sciences Pharma Biotech Consulting, and John Johnson also presented sessions at the event. John presented What Organization Behaviors Drive Perpetual Adherence to cGMP? While Pete presented Brexit – The Potential Impact for Pharmaceuticals.

If you would like a copy of the presentations, just get in touch with petegough@nsf.org or johnjohnson@nsf.org

To view the article from the event, look for 'What Are the Key Challenges to the Pharma Industry Right Now? You Told Us' under the 'other' section in our resource library: www.nsf.org/info/pblibrary

QP News and Updates

Royal Pharmaceutical Society's 15th Joint Qualified Person Symposium

The Royal Pharmaceutical Society, Royal Society of Biology and the Royal Society of Chemistry held their 15th Joint QP Symposium in May this year. NSF was pleased to sponsor the event once again and be part of a continually successful annual meeting that provides a forum for discussion about the latest changes, current issues and the latest news from the MHRA as well as the opportunity for valuable networking. It is essential to the role of the QP that meetings such as these allow past, present and future QPs to come together to share best practices, learn from each other and interact with regulatory bodies.

NSF continues to offer a very successful and interactive QP training program for those looking to gain QP eligibility and works with each individual delegate to guide and support them every step of the way. So, if you are considering QP training for yourself or any of your colleagues, we would be delighted to help.

NSF Funding Supports Research of New and Better Medicines



NSF's collaboration with the University of Strathclyde (UoS) started back in 1990 to deliver a program of training for those considering becoming a QP. The Strathclyde Institute of Pharmacy and Biomedical Science (SIPBS) offer many accredited degree courses including postgraduate certificate/diploma/MSc qualifications in

Pharmaceutical Quality and Good Manufacturing Practice. Our QP training program is an MSc-based course so our trainee QPs can attain these additional qualifications, if they wish, as they progress through the program.

The SIPBS is a top school of pharmacy, currently ranked second to Cambridge in the Pharmacy and Pharmacology league tables and is also a leading center for research. NSF continues to support their research of new and better medicines through funding raised from the QP training program.

From the NSF/UoS QP program, NSF is able to support seven different Ph.D. projects covering a wide range of specialist research. This includes nanoparticles in treating kidney disease and cancer therapy, pulmonary disease treatment, novel drug delivery and tissue engineering projects and much more.

For more information on the UoS, visit www.strath.ac.uk or to find out more about our QP training, visit www.nsf.org/info/qptraining

NSF Delegate QP VIVA Successes 2016 Passes

Ethan Baldry	Ann Marie Doyle
Richard Branton	Lee Mileham
Nicholas Clarke	Suzanne Moore
Beth Halliday	Helen Neal
Kay Hukin	Caroline Norfolk-Shaw
Anton Jarvis	Kate Waterhouse
Paul Jaynes	Colin Waugh
Alison Jordan	Krystyna Woodward

2017 Passes

Alan Clarke	Matthew Parkin
Lewis Corbett	Anne Radmall
Nisha Ghedia	Mahboob Rehman
Ian Pardo	Richard Sayer



NSF Staff Updates

A key characteristic of a high-performing team is that it is always looking to improve and grow to better serve customers and meet future demands. The NSF team has seen some updates throughout 2017, and we would like to introduce our new Executive Director, Director and Associates.



Lynne Byers, Executive Director

Lynne has extensive pharmaceutical manufacturing management and QA experience gained over 35 years working for three major international companies. In addition she has worked as the Head of Inspectorate and Licensing for the MHRA. Lynne has an excellent understanding of the EU GMP regulations, is eligible to act as a QP and has broad experience with the manufacture of a wide range of parenteral and non-parenteral dosage forms.



David Waddington, Director

In a career spanning more than 30 years, David has broad experience in QA and manufacturing management with three major international pharma companies. He has worked with a wide range of dosage forms for the global supply including solids, liquids, sterile products, food supplements and natural products. David is eligible to act as a QP and is fully conversant with current EU and FDA GMP regulations and requirements.



Eric Dewhurst, Associate

Eric Dewhurst has spent most of his career working with sterile pharmaceuticals and medical devices. Eric has held senior positions in microbiology, validation, quality assurance and regulatory compliance in a number of major companies, also acting as an EU Qualified Person. He has extensive experience with the MHRA inspecting plants manufacturing sterile products.

Louise Mawer, Associate

Learn a bit about Louise and why she chose to work with NSF in the Associate Spotlight on page 22.



Ian Ramsay, Associate

Ian joined the industry in 2004 and most recently worked for the MHRA, where he spent four years as a GMP Inspector inspecting many sites of varied dosage forms worldwide. Ian also has significant experience within QC and QA, spending time in frontline QA roles supporting a range of products and dosage forms including steriles, non-steriles, tablets, capsules, topicals, injectables, inhaled products and biologics.



Robert Smith, Associate

Robert is a qualified pharmacist, QP and vice-chair of the Royal Pharmaceutical Society's QP Eligibility Panel of Assessors. He has spent over 25 years working in the pharmaceutical industry, in both clinical trial supplies and the commercial sector. His current interest is in biological products including vaccines and advanced therapeutic medicinal products.



Associate Spotlight: Get to Know Louise Mawer



We spoke with Louise to learn a bit more about her and why she chose to work with NSF.

What is your working background?

"I have over 18 years' experience in the industry, including seven years as an inspector at the MHRA. I am a quality assurance auditor with extensive experience in GCP, GLP and more recently Good Pharmacovigilance Practice (GVP). Working initially in formulations research and development, I gained GMP experience and knowledge which has proved useful in both pre-clinical and clinical settings."

So, what made you want to work with NSF?

"For quality, content and delivery, NSF has a solid reputation for training as well as other key services and I'm excited to be a part of this team. Training is something I am really interested in and I'm hoping to broaden NSF's overall capabilities in process validation, GCP and GLP – helping to make NSF a one-stop shop for clients' training needs."

What do you think are the most interesting challenges facing our work now and in the future?

"It's the constantly changing regulatory environment, which is likely to get even more interesting over the next five to 10 years."

So, Louise, tell us a bit about yourself. Where are you from and what are your interests/hobbies outside of work?

"I currently live in Utley, West Yorkshire with my husband, but I'm originally from Halifax. I love to play the cello and have been learning for many years! I'm into 1930s and '50s fashion, and love to get tailor-made 1930s outfits. I enjoy traveling and I've got an obsession with Harry Potter!"

It was great to meet with Louise and we wish her all the best in her career with NSF.

We are always looking for new high-caliber colleagues (including Associate Directors, Directors, Executive Directors and Associates). If you think you have what it takes or would like more information, please contact mikehalliday@nsf.org

Advanced Program in Pharmaceutical Quality Management – Bangalore, India

Over 45 people have signed up for this world-class, MBA style **education program**. The first series of five modules will start this September and is designed to produce world-class quality, manufacturing and business leaders for the Indian pharmaceutical industry. If you can't start the first module in September, don't worry, you can join at any time.

Contact Martin Lush for more information – martinlush@nsf.org

NSF IN THE COMMUNITY – CHARITY WALK

The NSF team in the UK recently completed a beautiful 22-mile coastal walk to raise funds for the Multiple Sclerosis Society Ryedale Branch and Next Steps Mental Health Resource Centre. The team started off in Whitby, a small town in North Yorkshire, climbing the famous 199 steps up to Whitby Abbey before continuing along the coast, taking in the scenic views during the 22 miles to Scarborough. Although the team suffered from some big blisters, luckily it was a sunny day with everyone enjoying and finishing the walk!

Over £500 (\$650) was raised for the charities. Well done to everyone in the NSF team who completed the walk.



Forthcoming Courses

What's planned for October to December 2017



WORKSHOP | Good Distribution Practice

October 2 – 3, 2017

York, UK

Course Fee: £1390 excl. VAT

Pharmaceutical Legislation Update: Continuing Professional Development for Qualified Persons & Technical Personnel



October 3, 2017

York, UK

Course Fee: £770 excl. VAT

WORKSHOP | Good Clinical Practice

October 11, 2017

York, UK

Course Fee: £695 excl. VAT

Pharmaceutical Law and Administration



October 16 – 20, 2017

York, UK

Course Fee: £3395 excl. VAT

Free QP Seminar for Prospective QPs and Sponsors

October 17

York, UK

Course Fee: FREE

Pharmaceutical GMP Audits and Self-Inspections



(An IRCA Certified PQS Auditor/Lead Auditor Course)

October 30 – November 3, 2017

Amsterdam, Netherlands

Course Fee: £2880 excl. VAT

GMP for Clinical Trials Manufacture and Supply



November 6 – 9, 2017

Amsterdam, Netherlands

Course Fee: £2670 excl. VAT

Pharmaceutical Legislation Update: Continuing Professional Development for Qualified Persons & Technical Personnel



November 7, 2017

Milan, Italy

Course Fee: €625 (AFI member) / €690 (Non AFI member)

Analysis and Testing



November 13 – 17, 2017

York, UK

Course Fee: £3395 excl. VAT



WORKSHOP | Good Pharmacovigilance Practice

November 13, 2017

York, UK

Course Fee: £695 excl. VAT

Pharmaceutical GMP

November 20 – 23, 2017

Amsterdam, Netherlands

Course Fee: £2300 excl. VAT

A-Z of Sterile Products Manufacture



November 27 – December 1, 2017

Amsterdam, Netherlands

Course Fee: £3000 excl. VAT

WORKSHOP | Internal Auditor Training

November 30 – December 1, 2017

York, UK

Course Fee: £1390 excl. VAT

FREE WEBINARS

Leadership 2030 – What will it Take?

October 30, 2017

Performing Under Pressure

November 13, 2017

Conquering the Chaos – How to Thrive in an Uncertain World

December 4, 2017

Early bird or multiple delegate discounts apply to some of our courses. Please contact us for full details on all our available discounts.

For more information, email pharmacourses@nsf.org or visit www.nsf.org/info/pharma-training

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.

Streamlining the Pharmaceutical Quality System

What we found

- > The structure and function of a pharmaceutical quality system (PQS) were not well understood; the PQS was disengaged from the business and seen as a business obstacle
- > The PQS contained 2,300 policies, SOPs, instructions and records with multiple GMP documents for single processes
- > The site struggled with multiple GMP deviations, repeat regulatory audit observations and suspected data integrity issues due to staff finding it difficult to follow the documented instructions
- > Batch and GMP record 'right first time (RFT)' was <70 percent and contributed to the lagging release lead times and poor schedule adherence
- > Quality director and QP were seen as 'law enforcement officers'

What we left after NSF simplification

- > Identified 200 SOPs that could be deleted immediately and reduced cross-references
- > Identified 50 high complexity SOPs that were causing 80 percent of the GMP deviations and reduced the number of pages by 60 percent by using symbols, color, diagrams and photos
- > Trained 20 critical position holders on how to simplify process instructions and SOPs, and produced a custom toolkit to ensure each team member simplified at least 10 SOPs each year
- > Reduced the number of test methods and specifications by 60 percent using process mapping

Steps taken: How was this achieved?

- > Created the 'burning platform' that motivates document owners to take charge of their GMP documents
- > Trained and hosted simplification workshops targeting high complexity, high impact SOPs, instructions and records
- > Installed meaningful leading indicators for documentation 'RFT' and shared them widely

- > Mapped the PQS against ICH Q10, FDA QSIT 7356.002 and other cGMP references to look for gaps, overlaps and duplication
- > Trained and installed practical guidance on how to establish internal customer relationships

Tools used

- > Fedex days (24-hour exercises in innovation) to select processes best suited for simplification; allowing the biggest impact for the widest group of people
- > Process flow charting and swim lane diagrams
- > SOP simplification and model plans, checklists and routing/gateway charts

Return on investment

- > Over the course of two years, the number of GMP documents was reduced to 1,650, i.e. a 28 percent reduction in the documentation burden
- > RFT for batch records grew to >85 percent and batch release lead times dropped on average by seven days, driving a corresponding drop in 20 percent of finished product inventory
- > GMP non-compliance and client audit observations were reduced, including the site achieving its first blank FDA 483

Behaviors changed

- > The quality group became integrated into the business and is now seen as a facilitator
- > The company spun off a new project concerning cost of quality – known as 'war on waste'
- > Visibility of priorities and critical process steps led to more staff ownership, less tolerance of waste and more engagement in making valued change without fear of being overcome by the inertia or complexity of the PQS

Key message

Always drive simplicity and reduce the number of SOPs to improve the PQS



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