Journal

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The right people. The right solution. The first time.™

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Make 2016 Your Year of **PREVENTION – Not Reaction**

NSF® Health Sciences Pharma Biotech Consulting

30 YEARS

30 Years of Patient Protection

welcome

We can make your 2016 LESS STRESSFUL!

Firstly, a very happy New Year to you all! The beginning of every new year always encourages you to reflect on the past and make new commitments for the future. ***We implore you to make 2016 your year of PREVENTION***. Why? Because we've witnessed the consequences if you stay habituated (even addicted) to firefighting. Your business will eventually crash and burn. And so will you. The long-term impact on your health, family and personal relationships can be devastating. If you are caught in this downward spiral of firefighting you know that everyone loses…unless you decide to act differently. At NSF we've been in your shoes. We know what it's like. We also know how to fix it… by following the practical steps in this journal:

> Our Tech Talk column provides you with simple and practical guidance on **changing GMP behaviors**. Just follow the five key steps. You will also find information on our forthcoming courses, all designed to improve workplace behaviors.

> If you want to reduce your **documentation errors**, just read on. Need to reduce your **repeat deviations?** We tell you how. **Responding to regulatory agencies** after a tough inspection? Just follow our checklist. Want to **avoid data integrity issues?** Find out how. Wondering about the role of leadership in moving from crisis management to prevention and improvement? The answers are all in this issue.

> Our **free of charge 2016 webinar program** topics were chosen by you. These 30-minute sessions are designed to make your life easier and less stressful. Book now. They filled up within hours last year. To listen to our 2015 webinars, just follow this link **www.nsf.org/newsroom/pub-type/webinars/category/pharma-biotech** or scan the code alongside to get quick and simple advice.

You can also **follow me on LinkedIn** for information on error reduction, removing blame and other subjects all designed to help reduce your stress levels. We have also produced a series of five-minute videos covering best-in-class practices relating to human error, remediation, reducing repeat deviation incidents, risk-based decision making and lots more. Just scan the code alongside or follow this link **www.nsf.org/newsroom/pub-type/videos/category/pharma-biotech**.

Although we're regarded as the best at remediation (helping clients successfully manage severe regulatory action), we are also great at providing the support you need to STOP needing remediation in the first place. So, for those of you caught in destructive firefighting, you have a choice. Watch your business burn to the ground or read on and focus on prevention. When the climate gets too hot, please give us a call. We will help you.

Martin Lush

NSF Health Sciences Pharma Biotech Consulting

Martin Lush
President, NSF Health Sciences Pharma Biotech Consulting

Tech Talk

CHANGING GMP BEHAVIORS

by Martin Lush, President, NSF Health Sciences Pharma Biotech Consulting

Over 35 years' experience in operations, QA, troubleshooting and due diligence. Now committed to helping clients do better with less.

> *"Human behavior flows from three main sources: desire, emotion and knowledge."*
>
> – Plato

Here's a quick quiz for you…

- How many New Year's Eve resolutions are forgotten within a few days. Hours even?
- How many traditional training sessions fail to improve workplace behavior?
- How many culture change initiatives do little more than improve the bank balances of the change consultants?

The answers are… most of them. According to Blanchard et al. and the Harvard Business Review, upwards of 70 percent of change initiatives fail. In fact, they often leave organizations worse off. The added confusion, uncertainty, complexity and cost all eventually add up. The good thing is that it doesn't have to be this way. The latest research confirms what Plato already knew. The way people behave comes down to three things: their motivation, ability and habit.

Behavior at its simplest level = MAH

Motivation

Most people are content sticking with what they know and their tried and tested habits. It's easy. To get people to think and act differently (a painful process for most), you have to provide them with the motivation.

- What's in it for them?
- How will their lives be better?
- Why should they really bother?
- What difference will the behavior make?
- What could go wrong if they don't? What are the risks?

No personal motivation = no behavioral change = no cultural change. Don't use corporate language or management speak, which usually has the opposite effect. Motivation to think and act differently has to be personal, emotional and desirable.

Ability

To change behaviors you must provide people with the:

- Education and underpinning knowledge (the why)
- Skills training (the how)
- Tools, systems and procedures required

You must also remove barriers – anything and everything that prevents adoption of the new way of working – to the new GMP behavior.

Inappropriate KPIs, old SOPs, poorly designed equipment and old management attitudes can all kill any change initiative stone dead!

Habit

A habit is an automatic act. Through repetition and precise practice we do things without thinking, like sanitizing/washing our hands, no matter what.

To change ways of working, you have to replace old habits with new ones. If you attended our free webinar (listen any time at **http://bit.ly/1lax9MV**) you know the vital importance of the habit loop – having a cue or trigger for the new behavior, followed by a simple (robust) routine followed by a reward that encourages people to repeat the new behavior.

So, if you are interested in changing GMP behaviors, here are your "five to drive:"

Step one:	Identify the ***specific*** behavior you want to change
Step two:	Identify what drives the old behavior
Step three:	Provide the motivation for the new behavior
Step four:	Provide the right tools, systems and procedures
Step five:	Create the new habit

Case Study: How NSF helped a client to change GMP behaviors generating $ millions in savings

In the manufacture of sterile products, adopting good aseptic practice really matters. This is how operators in the Grade A areas (Class 100) interact with the product and process. Poor aseptic practices = increased risk of contamination = risk reduced assurance of sterility. One vital part of good aseptic practice is the routine sanitization of operators' gloved hands, every time they move between Grade A and Grade B. This must become a vital habit.

When the client came to us, it was experiencing…

- Inconsistency in glove sanitization practice. Most sprayed their hands, but differently. Some operators simply forgot
- Adverse trends due to bacteria being found on the gloved hands during routine monitoring
- Very costly investigations and, even worse, batch rejects

Our client did its best to fix the situation, but the additional training, signature checking and SOP amendments only made the situation worse.

We then took the client through our five step process which has, over the first six months, saved many $ millions in direct and indirect costs.

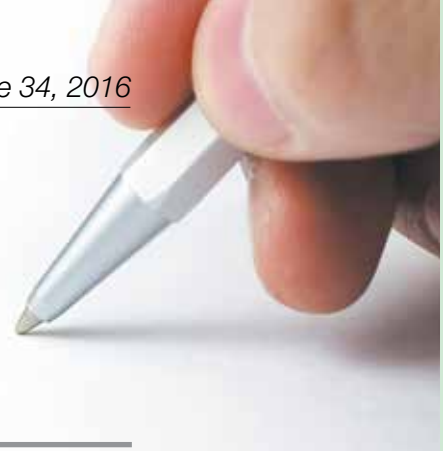
Step One: Identify the specific behavior you want to change

The behavior was defined as "Ensure operators spray their hands in a consistent manner each and every time they move from Grade A to Grade B and back".

Step Two: Identify what drives the old behavior

We spent many hours with the operators to understand their world and what was driving their old, inconsistent behaviors. This is what we found:

- Some were totally unaware of the vital importance of effective sanitization. They had been trained in the how (follow the SOP) but not educated as to the why or, importantly, the consequences of getting it wrong (contaminated product!). They were not risk aware
- The SOP was overly complex, confusing and impossible to follow
- Operators were rushing due to production pressures



- The sanitizer spray bottles were never in the same place
- Some operators simply forgot, even though they had been trained
- Poor design of sanitizer bottle made it difficult to use

Step Three: Provide the motivation for the new behavior

The team needed education to help them care more, so we took them into the micro lab. We showed them pictures of what microbes can do to people. We talked about the limitations of the sterility test and introduced them to the world of the microbe. We explained how just one microbe can kill a susceptible patient. They took lots of samples from their hands before and after washing with and without gloves. We then covered their hands with a fluorescent powder before they sanitized them. With the help of a UV light we showed them the contamination they had missed. They looked at microbes on the agar plate and down the microscope. After a few hours they emerged very motivated. For the first time they understood the risks (the "why bother"). For the first time they were emotionally engaged with what they had to do.

Step Four: Provide the right tools, systems and procedures

In just one day the operators…

- Agreed on a standard process for glove sanitization
- Practiced and refined it until no florescent powder remained after washing
- Ripped up the six page SOP and replaced it with a one-page checklist, with just five action points – their action points
- Printed checklists on highly visible (yellow) laminated paper and placed them on the walls next to the sanitizer. You couldn't miss them!
- Replaced the old hand spray with one easier to use

These improvements were driven by the users, not by management. For example, the checklist was considered (by some who had not been involved) to have insufficient detail to satisfy an auditor. We pointed out that its role was to provide essential guidance to an operator, not the auditor. Thankfully we won the day!

Step Five: Create the new habit

- We talked them through the habit loop so they could design their own triggers and rewards without which new practices and behaviors don't become routine
- They placed red pictures of the sanitizer bottle on the LAF units to act as a trigger or reminder
- Sanitizer bottles (also in red) were placed in standardized locations
- Because they were so motivated, they provided each other with immediate feedback and coaching when poor practice was observed. They regularly checked effectiveness using the fluorescent stain challenge

The Rewards: Return on Investment

By following our "five to thrive" process, in just six months our client generated $ millions in savings through reductions in repeat deviations and rejected batches, achieving:

- Reduced SOP non-compliances by 98 percent
- Lowered batch rejects from three per year to zero
- Dramatically reduced deviation incidents
- Improved aseptic practice and therefore patient safety

If you would like to benefit from a customized workshop on improving GMP behaviors, please give us a call. What you learn could transform your GMP compliance.

Sick of Firefighting?

by

Martin Lush,
President, NSF
Health Sciences
Pharma Biotech
Consulting

Make 2016 Your Year of PREVENTION, Not Reaction…for the Good of YOUR Health

At NSF we understand the pressures you're under and the challenges you face. We've all been in your shoes. We know that a culture of reactive firefighting has nothing going for it at all. It consumes energy and resource and gives the illusion of progress. It's stressful and exhausting as well as being addictive. Firefighting burns you out and ultimately destroys your business. We have a challenge for you. **Make 2016 your year of PREVENTION:**

2016: NEW YEAR – NEW START

From firefighting → Fire prevention
From crisis management → Predictable control
From risk of regulatory criticism → Happy investigators
From high cost of poor quality → Cost reduction
From drug shortages → On time in full, with no stockouts

At NSF we're lucky in having the best brains in the business. Most of our team members have an average of 30 years' industry experience. We have a range of experts from ex-regulators to seasoned industry professionals. Well, we've brought this expertise together to help make your 2016 different. We are here to help you move from expensive and unsustainable firefighting to prevention and prosperity. Our research suggests that these are the top six areas for a step change in performance next year:

1. Documentation Errors
2. Audits and Self-Inspections
3. Deviation and CAPA Systems
4. Inspection Responses
5. Data Integrity
6. Leadership

We believe your success comes down to doing these basics exceptionally well. For each of the above we have provided you with:

- ☑ The Why – Describing why excellence in each area is so vital
- ☑ Your "Six To Fix" Right Now – Basics you need to do exceptionally well
- ☑ How NSF can help to ease your pain, generate savings and reduce your risk by making 2016 a year of prevention. A New Year …a New Start

Documentation Errors

by

John Johnson, Executive Director, NSF Health Sciences Pharma Biotech Consulting

Jim Morris, Executive Director, NSF Health Sciences Pharma Biotech Consulting

The Why?

"Right first time" means less rework, less re-inspection, fewer deviation investigations, less waste and lower risk of defective product on the market. Doing a job properly and to the right standard is a basic human need, and disorganized working practices disengage your best staff and stifle any attempt at business improvement. But right first time does not happen by accident; it is a result of good design, effective controls and a management culture that makes war on waste.

Your "Six To Fix" Right Now

1. Identify the critical position holders in your organization and invest your time and resources in making their best even better; making it a basic job requirement to prevent the eight forms of waste in any task assigned to them
2. Coach your key staff to be alert and intolerant of risk; but be careful to focus only on the risks that truly affect product quality, patient safety, product availability and unacceptable cost
3. Map your most time-consuming or complex processes and allow your staff to tell you where issues, delays and non-conformances occur; then listen and act!
4. Make simplicity a virtue; reward simple solutions and question complex solutions – remember that easily defined processes are also easy to keep in a perpetual state of GMP compliance
5. Your products are defined by the GMP documentation that supports the decision to release them to market. Are these documents accessible and being followed explicitly?
6. Who owns your processes and the associated documents? Have you made it obvious to them that you value simplicity, speed and flawless execution? Do your measures define success?

How NSF can help to reduce complexity, non-conformity and budget over-runs?

> Allow us to coach your critical position holders on how to manage the cost of producing product to the right quality, at the right time and to pre-determined budget

> Use us to gain a critical insight in what your competitors are doing to edge you out of the business – e.g. how do they shorten lead times for new product introductions and as a consequence get their assets returning revenue far sooner than you can

> Use our seasoned professionals to seek out areas of waste and frustration, and then work out simple strategies to eliminate them

> Use us to guide your team on how to use risk-based decision making when faced with issues that have no black or white option. Investing in the skills of decision making is proven to prevent waste and rework. No one wants to experience Groundhog Day

> Our human error reduction program has been run worldwide and has made an enormous impact in reducing the risk of costly, unpredicted and sometimes devastating human error

> Allow us to customize a program of coaching, tools and processes (specific to your business or technology), dedicated to simplification, error reduction and waste management

> We know how competitive the industry is and that time is at a premium. Let us help you to avoid expensive distractions that steal your time and attention away from those things that really matter

For more information please contact John Johnson at **johnjohnson@nsf.org** or **+44 (0)1751 432999** or Jim Morris at **jmorris@nsf.org** or **+1 202-342-3618**

by

Mike Halliday,
Vice President,
NSF Health Sciences
Pharma Biotech Consulting

Audits and Self-Inspections

Nothing protects your business like self-inspections (internal audits)!

Or at least that's the theory. The internal audit or self-inspection system together with the senior management quality review are the two main systems that drive continuous improvement and more importantly provide an indicator of how well a company is complying with its own quality system and regulatory requirements. It is the one main system that protects a company from regulatory failure. In many companies the importance of the internal audit system is grossly underestimated and under resourced. Regulatory inspections would not find any deficiencies if the internal audit system were working perfectly! Internal audits should review all elements of the quality system including the senior management activities relating to it. If the internal auditors are trained, competent and given the authority, the resources and a well-defined system to do their job properly, all gaps, weaknesses and non-compliances should be found.

Each year we train over 250 people through our IRCA Certified Lead Auditor Course, Pharmaceutical GMP Audits and Self-Inspections. On this course we explore the similarities and differences between self-inspections and external audits. Too often the message is that while all agree that there are more similarities than differences, there is less interest in the outcome of internal audits. Of course internal audits can range from a review of a line or processes or system to a site-wide corporate audit or review with all the politics and sensitivities involved in the site-to-site comparison.

The real value of internal audits is the knowledge brought by the auditors of the company products, processes and systems. Knowledge of products and processes helps focus on what is important to that product and patient (ICH Q8), where the risks are in the process' supply chain or system (ICH Q9) and how the whole process fits into the QMS with management overview and provision of resource (ICH Q10). A little simplistic but it does provide an opportunity for a more holistic audit process than any external overview.

One of the most positive messages I've come across recently was in discussing auditor training with a FMCG/pharmaceutical company. Internal auditors were actually titled "continuous improvement assessors." That seemed to me to sum up the best ethos: Well-trained, highly experienced auditors trained to protect the business and its patients and to drive continuous improvement. Perhaps we are getting better after all!

"Six to fix" to create effective internal audits:

1. Encourage a culture of audits as value-adding improvement opportunities
2. Train auditors in quality systems, processes and audit technique
3. Encourage a culture of risk-based auditing to address risk to patient and business
4. Provide senior management support for the internal audit process, not to punish but to improve
5. Review findings from external audits by inspectors and clients as feedback on the effectiveness of the internal audit process
6. Realize that every system can be improved including the audit system itself

How can NSF help:

> Help all your auditors to become the best they can be through auditor training

> Provide pragmatic tools and techniques for auditing that work

> Provide experienced auditors to accompany your internal auditors to mentor and guide in the planning, preparation and performance of the audits

> Benchmark your audit systems against the norms and best practices we see

For more information please contact Mike Halliday at **mikehalliday@nsf.org** or **+44 (0)1751 432999**

Deviation and CAPA Systems

by

Martin Lush, President, NSF Health Sciences Pharma Biotech Consulting

Andy Barnett, Director, Quality Systems, NSF Health Sciences Pharma Biotech Consulting

The Why?

Your deviation and CAPA system must do two things exceptionally well: manage your risks and drive continuous improvement. Whenever something goes wrong or the unexpected happens, you have to quickly assess impact (risks) and ensure you prevent the incident happening again. Remember, success depends on learning from your mistakes.

Your "Six To Fix" Right Now

1. Make sure you have a culture that allows errors to be reported without fear and without delay. You need an organizational mind-set that sees errors and mistakes as rich learning opportunities, not as painful inconveniences
2. Ditch the 30-day rule (if you have it). Investigate as quickly as possible at the scene of the incident, never from behind a desk. The quicker you get there, the better the investigation
3. Investigate proportionate to risk; treating every incident the same is dangerous
4. Focus on trends and behaviors, not necessarily individual incidents
5. Make sure 80 percent of your actions are preventive, 20 percent corrective (risk containment)
6. "Certify" your investigators of deviation incidents. Make sure they know how to use their problem solving tools and techniques correctly and that you see reductions of repeat incidents

How NSF can help to reduce repeat incidents:

> We can help you save $ millions by identifying the 20 percent of common causes that lead to 80 percent of deviations so that repeat incidents are a thing of the past

> Our education programs, customized to meet your exact needs and requirements, will provide simple problem solving tools and techniques that work

> Simplification. We can work with you to streamline your deviation and CAPA system so your investigations are quicker and more efficient, allowing you to do more with less

> Our unique course on Human Error Prevention will reduce your incidents due to so called human error

> Benchmarking. Want to know how you compare with the best in class? We can tell you what you need to do and, importantly, STOP doing

For more information please contact Andy Barnett at **abarnett@nsf.org** or **+1 202-828-1589** or Martin Lush at **martinlush@nsf.org** or **+44 (0)1751 432999**

Inspection Responses

by

Maxine Fritz, Executive Vice President, NSF Health Sciences Pharma Biotech Consulting

Rachel Carmichael, Executive Director, NSF Health Sciences Pharma Biotech Consulting

Responding to a regulatory authority can be an intimidating task even for the most experienced pharmaceutical veteran. To make this task easier, follow our tips and use our checklist for every step from the "discussion with management" to submission of the response.

The Why?

Your inspection response is a permanent mark of your company. It identifies whether you are taking the subject of compliance seriously. The inspectors are there to protect the public health and take this very seriously. Responses can sometimes be:

Overly defensive This indicates that you may not understand the requirements or you don't believe your inspector does, neither of which is desirable

Too weak Failing to address the root cause of the issue can indicate that you don't understand the GMP requirements of a quality system

Your "Six To Fix" Right Now

1. Make sure you fully understand the finding! Read the reference that the inspector has provided for the deficiency and make sure that the response addresses what was raised
2. Respond to all of the finding. Make sure you explicitly address each of the sub-parts of a deficiency. Look at the issues holistically and ask yourself if it is a systemic problem
3. Don't try to defend your current practice. The inspection established the deficiencies and the closing meeting was your opportunity to comment. Now is the time to address what has been found – not to defend your current practices
4. Identify the root cause and address it enterprise-wide
5. Introduce a formal system to identify and address current requirements – too often deficiencies are due to a failure to update systems in line with current requirements
6. Set a time frame for action completion that reflects the severity of the deficiency, track delivery and communicate any slippage openly and before the inspector discovers it

How NSF can help to improve your inspection responses:

NSF Pharma Biotech Consulting is a full-service quality systems and regulatory consulting company with a team of regulatory and industry experts who:

> Help you to prepare, write and review the regulatory responses with your team of experts

> Help you develop appropriate work plans and corrective action plans

> Help you remediate the corrective actions through sound industry and regulatory expertise

> Can staff very small or very large projects quickly, minimizing disruption to site activities

> Have training programs that can teach your staff how to solve problems, develop investigations and determine the root causes

> Can help you to prepare for the next regulatory inspection through mock inspections, help to manage your regulatory inspections and provide auditing to ensure regulatory compliance

For more information please contact Maxine Fritz at **mfritz@nsf.org** or **+1 202-828-1585** or Rachel Carmichael at **rcarmichael@nsf.org** or **+44 (0)1751 432999**

INSPECTION CLOSE-OUT AND **RESPONSE** WRITING CHECKLIST

1. THE INSPECTION CLOSE-OUT DISCUSSION WITH MANAGEMENT

- ☐ Make sure you have the appropriate personnel available including the person designated most responsible for handling all matters concerning the close-out
- ☐ Make sure that you correct inaccuracies and ask the regulatory authority to annotate; now is not the time to argue points
- ☐ Limit conversation unless pertinent to the findings
- ☐ Take detailed notes
- ☐ Promise to respond in writing to the findings within the required response period
- ☐ Confirm with the regulatory authority to whom and where the response should be sent

2. AFTER THE CLOSE-OUT

- ☐ Immediately assemble a cross-functional team of experts depending on the findings
- ☐ Determine when the response is due, consider holidays when factoring time and remember the due date
- ☐ Designate a lead person for each observation who will be responsible for speaking to the subject matter experts and determining the appropriate corrective actions
- ☐ Provide by the next day a response format/template including observation/response and timeline for corrective action completion
- ☐ Ask for the initial response in five days or less; you will need time for management to review and to finalize your response and prepare the submittal, cover letter, documents and any records
- ☐ Set up daily meetings to see how the team(s) is (are) doing with the response
- ☐ Keep control of the response master

3. RESPONSE STRATEGY

- ☐ Meet with management to understand the inspectional observations; use the findings and your daily notes from the inspection to guide you
- ☐ Address any safety issues and determine the risk to patient by conducting a risk assessment if one doesn't already exist

Continued overleaf

- [ ] Look for systemic corrective/preventive actions when addressing the findings; they may not always apply, but you need to evaluate
- [ ] Understand and identify the resource requirements for the commitment to establish the timeline for completion – what is needed, a CAPEX, resources, validation, qualification, etc.

4. RESPONSE WRITING

- [ ] Assemble the response from the team and review any documentation and records
- [ ] Always address the issues, correct factually incorrect errors and be prepared to provide documentation
- [ ] Don't address just the issue, but look for system solutions that will be sustainable
- [ ] Provide a realistic timeline; the regulatory authorities really do know how long it should take so don't promise too quickly or take too long
- [ ] Depending on the severity and type of issues, seek outside assistance; hire a third party and let the regulatory authority know you have done so
- [ ] Show your commitment to correct by your corrective actions; actions speak louder than words and the regulatory authority will verify your response commitments on re-inspection
- [ ] Meet with management to make sure they are fully informed of, agree to and support, the commitments and promises being made; **management is ultimately responsible and has the authority to effect change**

- [ ] Write a cover letter to the regulatory authority for management to sign with a commitment to correct; if applicable promise to provide monthly or quarterly updates (not all responses require this level of communication)
- [ ] Check with the inspector or regulatory authority on how they will accept the response (email, CD or hard copy) and submit your cover letter, response to the findings and any document and records on time; they must be received, not sent, by the due date

Data Integrity

by

Rachel Carmichael, Executive Director, NSF Health Sciences Pharma Biotech Consulting

George Toscano, Senior Director, Quality Systems, NSF Health Sciences Pharma Biotech Consulting

The Why?

For another year running, data integrity remains one of the hottest of "hot topics!" A fundamental building block of our operations, records are worthless if not created in a structure which demands compliance with honest and transparent record keeping – who did what, where, when and why. There is nothing clever or magical about this – it is not a new discipline but about doing the basics of GMP record keeping properly and ensuring that the requirements are met regardless of the format the records are presented in.

Your "Six To Fix" Right Now

1. Ensure leadership buy-in; senior management must:
   a. Set an example and promote data integrity
   b. Challenge the quality management system to ensure it is working
   c. Ensure adequate resources and workload expectations to avoid creating pressure situations for analysts and operators to create system shortcuts
2. Make sure you have a data governance system that:
   a. Provides an acceptable state of control based on the data integrity risk
   b. Is fully documented with supporting rationale
3. Ensure relevant policies are in place. What do you require and what will you do if issues are identified?
4. Have staff training address the importance of data integrity. Training must cover "why" not just the "what."
5. Understand and document the controls that are applied to different areas of your quality system include organizational (e.g. procedures) and technical (e.g. computer system access controls)
   a. Implement a robust qualification program to ensure that all data acquisition software is qualified and suitable for all functions employed, including data generation, storage, archival and retrieval
6. Make sure that your internal audit and supplier audit programs have fully considered potential issues and that key areas of risk have been thoroughly investigated

How NSF can help you with data integrity:

> We can train your staff to understand data integrity, the basis for the requirements and why this matters at an organizational and personal level

> We run courses at both introductory and detailed levels – focused on compliance with EU GMP Chapter 4 (Documentation) and Annex 11 (Computerised Systems)

> We employ experienced professionals with recent experience of GMP inspections and the issues associated with data integrity. They can give an inside perspective on how inspection questions may be posed, how issues may be viewed by regulators, how best to present potential issues and how you can best prepare for and execute the presentation of concerns

> We can provide data integrity-focused audits to pressure test your systems and help identify areas that require improvement as well as provide practical yet compliant solutions to address any deficiencies

For more information please contact Rachel Carmichael at **rcarmichael@nsf.org** or **+44 (0)1751 432999** or George Toscano at **gtoscano@nsf.org** or **+1 202-822-1850**

Leadership

by

John Johnson, Executive Director, NSF Health Sciences Pharma Biotech Consulting

Nicholas Markel, Executive Director, NSF Health Sciences Pharma Biotech Consulting

The Why?

Regardless of leadership style, strong leadership is imperative for long-term sustainable success and growth. Strong leadership shapes the corporate culture, defines goals and sets the ultimate example for all employees. With strong leadership comes motivated and enthusiastic employees, which will ultimately create a workplace that attracts and retains the very best employees available. Managing and leading are not the same thing. Managers plan, budget, organize and coordinate while leaders envision, create excitement, motivate and align the workforce. Excellent leaders will reduce the amount of fires that need to be fought and, when the inevitable fire pops up, will help you navigate and respond in such a way that the fire is put out for good.

Your "Six To Fix" Right Now

1. Develop your leaders. While some people might be born with innate leadership skills, everybody needs help. Leaders are not born; they are grown. Peter Drucker, Harvard Business Review: July 14, 2009
2. Develop a succession plan for every level of leadership
3. Select your leaders in a thoughtful manner. Don't just pick the next person in line with the most seniority
4. Focus on and invest in your floor leadership. These individuals should be among the finest in your organization and be supported as such
5. Encourage and allow your leaders to lead by keeping a "service heart" top of mind
6. Encourage and support your leaders to be creative

How NSF can help you understand your leadership needs and build and retain your leadership talent. We can help you:

> Develop tools to help you stay ahead of the leadership "demand curve"

> Determine the best leadership style for your company

> Identify leadership gaps and then identify new leaders to fill that gap

> Develop/refine position descriptions to highlight leadership needs – this is the easiest and most cost-effective way to ensure an uninterrupted supply of excellent leaders

> Develop a leadership development plan as well as a plan to retain those leaders

For more information please contact John Johnson at **johnjohnson@nsf.org** or **+44 (0)1751 432999** or Nicholas Markel at **nmarkel@nsf.org** or **+1 202-828-158**

Conclusion

Albert Einstein once said

> *"Insanity is defined as doing the same and expecting a different result."*

So, if you want to get a different result you have to do things differently. You have to do the basics exceptionally well. In this turbulent world only the resilient will survive. The survivors simply do the basics exceptionally well and they focus on prevention, not firefighting. The challenge for many is breaking the firefighting habit. If you want help, please give us a call for more information:

Our Consultancy services

Help you to simplify your deviation and documentation systems and improve your self-inspection programs

Our Benchmarking services

Will help you to implement best-in-class practices quickly and spend your money wisely

Our Education Programs

Customized as well as residential will transform performance in the following areas:

> Human error prevention

> Data integrity

> Deviation and CAPA: Problem solving and root cause analysis to drive down repeat incidents

> Advanced problem solving tools and techniques

> Simplification tools and techniques

> Pharmaceutical lead auditor certification (IRCA certified)

> Quality leadership

Our Expertise in Remediation

Helps you make the right decisions so that you emerge from adversity stronger and better prepared for the future

For more information about any of the services we offer, please contact **Martin Lush** at **martinlush@nsf.org** or **+44 (0)1751 432999**

Regulatory Update

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

40 years' experience in pharmaceutical law, manufacturing, QC and quality systems. Now helping our partners understand ever-changing regulatory expectations to remain compliant.

EU News

The final version of the revised Annex 16 was finally published on October 12, 2015 and becomes effective from April 15, 2016. This revision is a complete re-writing of this Annex. The reason for the revision is given as the need "to reflect the globalization of the pharmaceutical supply chains and the introduction of new quality control strategies."

The revised Annex has the following structure:

Scope

General principles

1. The process of certification
2. Relying on GMP assessments by third parties, e.g. audits
3. Handling of unexpected deviations
4. The release of a batch
5. Glossary

Appendix 1: Content of the confirmation of the partial manufacturing of a medicinal product

Appendix 2: Content of the batch certificate for medicinal products

The scope of the Annex covers all QP certification of human and animal medicinal products within the EU. The final version states that the principles of this guidance also apply to investigational medicinal products (IMP) for human use.

Regarding batch release, the revised Annex defines a three-step process:

i. The checking of the manufacture and testing of the batch in accordance with defined release procedures.

ii. The certification of the finished product batch performed by a QP signifying that the batch is in compliance with GMP and the requirements of its MA. ***This represents the quality release of the batch.***

iii. The transfer to saleable stock, and/or export of the finished batch of product which should take into account the certification performed by the QP. If this transfer is performed at a site other than that where certification takes place, then the arrangement should be documented in a written agreement between the sites.

The new text explicitly states "*If the QP is responsible for confirming compliance of those operations with the relevant MA, then the QP should have access to the necessary details of the MA.*" This clarification is important as QPs at contract manufacturers are not always provided with the necessary MA details by the contract giver.

The 2013 draft revision stated that the product must either undergo the required re-testing within the EU or be "*in accordance with an approved Real Time Release Testing programme.*" In the final version this reference to real time release testing (RTRT) has been omitted. It is unclear if any significance should be attached to the removal of this reference to RTRT in relation to re-testing on importation.

The major change in the final version from the 2013 draft lies in the requirements for the sampling of imported products. The 2013 draft stated sampling "*be taken after arrival in the EEA*". This provision has been reversed and the final version permits samples to be taken at the third-country site. However, if sampling in the third country is adopted, the Annex requires that this be technically justified and "*Any samples taken outside the EU should be shipped under equivalent transport conditions as the batch that they represent.*" The technical justification should include a formal, documented risk assessment.

The new Annex no longer contains the eight routine duties of the QP, which originally came from the UK's Code of Practice for QPs.

Instead, these are replaced by operational responsibilities that the QP must personally ensure are fulfilled:

1. Certification is permitted by the MIA
2. National legislation is complied with
3. Certification is recorded in a register or equivalent

There are a further 21 points that the QP has to ensure but these may be delegated to appropriately trained personnel or third parties. It is recognized that the QP will need to rely on a quality management system and the QP should have ongoing assurance that this reliance is well founded.

Section 2 deals with relying on GMP assessments by third parties, e.g. audits. It states that Chapter 7 of the EU GMP Guide should be complied with and gives detailed guidance on the content of audit reports. It also states that "*The QP should have access to all documentation which facilitates review of the audit outcome and continued reliance on the outsourced activity.*"

Section 3 deals with unexpected deviations. This section is similar to the guidance contained in the 2009 Reflection Paper in that it states that the registered specifications must all be complied with but, if this is the case, a QP may consider certifying a batch, providing that the specified risk assessment activities have occurred, where an unexpected deviation (concerning the manufacturing process and/or the analytical control methods) from details contained within the MA and/or GMP has occurred.

Section 4 deals with batch release. Until it is certified, the batch should remain at the site of manufacture or be shipped under quarantine to another site which has been approved for that purpose by the relevant competent authority. It requires safeguards to ensure that uncertified batches are not released.

Section 5 is a glossary of terms.

ICH News

In January 2015, following a meeting in Lisbon in the autumn of 2014, ICH published a new governance structure under a new legal entity. This new legal entity has now been set up as a non-profit association under Swiss law and the name changed from the International Conference on Harmonisation to the International Council for Harmonisation, which enables retaining the acronym ICH. This new structure consists of the following elements:

> ICH Assembly

- This is comprised of the ICH Management Committee and ICH members. It is the overarching body of the new association. The inaugural meetings of the new Assembly (and Management Committee) were held on October 23, 2015

> ICH Management Committee

- This committee is in charge of operational matters. It is primarily responsible for administration and financial matters. It initially consists of the existing (as of January 1, 2015) members of the former ICH Steering Committee, who have become permanent members. The current observers in the Steering Committee have become permanent observers
- After two years, new committee members will be elected by the assembly from the larger membership

> ICH Members

- ICH membership will be open to regulators and industry associations who meet specified criteria

Regulatory Update

After the inaugural meeting in October 2015, the new ICH Assembly declared "The fundamentals of what the ICH parties are trying to achieve are not changed, but the reforms to the process and organisation were needed to adapt to changes in how medicines are developed and regulated. These changes mark an exciting moment for us to help harmonise and streamline the global drug development process for the benefit of patients around the world."

PIC/S News

In October 2015 the Pharmaceutical Inspection Co-operation Scheme (PIC/S) held its committee meeting and annual seminar, which this year was hosted by the Indonesian National Agency for Drug and Food Control (NADFC).

The PIC/S Committee elected Mr Paul Hargreaves of the United Kingdom MHRA as Chairman for the period 2016 to 2017. The 2016 annual seminar will be hosted by the MHRA and held in Manchester in July.

Croatia (HALMED) and Hong Kong (SAR/ PPBHK) were accepted for membership of PIC/S and became the 47th and 48th members on January 1, 2016. Mexico and Thailand have applied for membership and join Brazil, India, the Philippines and Turkey as countries that are in the process of being assessed.

UK News

The Clinical Trials Regulations (536/2014) was published in May 2014 and will be implemented six months after the new application portal is available, which is not likely to be until 2017.

The Regulation brings a number of changes but one which may have the greatest personal impact to the UK Qualified Person population is the fact that there is no provision for Transitional Qualified Persons in these Regulations. This is largely a UK issue as most other member states did not use the transitional option when it was available to them. The MHRA has said they are conscious of the potential impact that this will have on the Holders of UK MIA(IMP) Licences and has announced that Transitional QPs (that were agreed in the UK under the SI 2004/1031 arrangements) will be re-assessed by the MHRA Inspectorate to ensure that they meet the full requirements of a Qualified Person as detailed in Article 49(2) and (3) of 2001/83 (as required by Article 61. 2 (b) of Regulation 536/2014). In essence these requirements are as follows:

> Article 49(2) states that the "qualified person shall be in possession of a diploma, certificate or other evidence of formal qualifications awarded on completion of a university course of study, or a course recognized as equivalent by the Member State concerned, extending over a period of at least four years of theoretical and practical study in [specified] scientific disciplines"

> Article 49(3) requires that the qualified person shall have acquired practical experience over at least two years, in one or more [specified] undertakings which are authorized to manufacture medicinal products

However, Article 49(2) goes on to say that if the evidence of formal qualifications does not fulfil the criteria laid down in this paragraph, the competent authority of the Member State shall ensure that the person concerned provides evidence of adequate knowledge of the subjects involved and it is this provision that the MHRA is looking to use. Successful applicants will be issued with an eligibility certificate. We recommend that all Transitional IMP QPs keep an active eye on the MHRA website and inspectorate blog for updates on this process.

News...

NSF Collaborates with FDAnews and FDA Representatives for Interactive Combination Product Workshop

Mary C Getz, PhD
Vice President, NSF Medical Device Consulting

Thought leaders in the combination product space, led by NSF Health Sciences, came together in Nov. 2015 in Bethesda, Maryland at an interactive workshop focused on regulatory requirements, challenges that manufacturers face and industry best practices. The workshop, "Combination Products Summit: Streamlining 21 CFR Part 4 Compliance," involved U.S. FDA officials John (Barr) Weiner, Associate Director for Policy and Product Classification Officer, Office of Combination Products; Dinesh Kumar, Regulatory Counsel, Office of Orphan Products Development, Office of Policy and Risk Management, ORA; Edward Patten, Associate Director Manufacturing Science, Office of Medical Products and Tobacco, Office of Compliance and Biologics Quality, CBER; Francisco Vicenty, Mechanical Engineer, Division of Analysis and Program Operations, CDRH; and Jay Jariwala, CSO, Combination Product Expert, OC, CDER.

The workshop was chaired by Mary C. Getz, PhD., Vice President of NSF Medical Device Consulting, leading speakers from industry: Johnson & Johnson, Abbott and Gore and drug and medical device industry consultants. Elaine Messa, President and Olivia Wong, Director, also represented NSF.

The workshop focused on highlighting areas within the QSRs or GMPs that may trip up pharmaceutical or medical device manufacturers as they establish and implement compliance to 21 CFR Part 4. Presenters delivered anecdotes from experiences of pharmaceutical manufacturers adding the medical device GMP requirements to move into combination products, and vice versa. Specific topics included: how and when to implement design controls, understanding laboratory controls, effective application of purchasing controls, best practices in managing CAPA and non-conformances and how management can sustain overall GMP compliance. Speakers led topical case studies and provided attendees with tools to develop quality systems.

The workshop is the first in a line of annual events, the next event expected mid-year.

Qualified Person (QP) Education Update in India

In Journal 33, our QP style education program launch in India was highlighted, in collaboration with the Indian Drug Manufacturers Association. Progress Report:

- To be called 'Executive Course in Pharmaceutical Quality Management (PQM)'
- Course content to satisfy EU study requirements for QP'
- Part time residential modular education program to be presented in Bangalore
- Containing ten modules, each module – 4 days duration
- Written assessment to accompany each module
- Presented by experienced, NSF UK staff

Target audience:

- Pharmaceutical professionals
- EU/US based multinationals who want to reduce business risk

Requirements:

Participants must have a science degree (Pharmacy, Chemistry, Biological Sciences) and a minimum of two years' experience in the Pharmaceutical Industry

NSF-IDMA to jointly award delegates a **Certificate in Pharmaceutical Quality Management** who successfully pass the rigorous written assessments.

More info? Contact Martin Lush (martinlush@nsf.org)

Forthcoming Courses

What's planned for March – September 2016

Our EU Career Path Key

- Active Pharmaceutical Ingredients/ Excipients
- Audit/ Self-Inspection
- Biopharmaceuticals /Biotechnology
- Clinical Trials/ Investigational Medicinal Products
- Good Manufacturing Practice
- Laboratory Management/ Quality Control
- Pharmaceutical Law/Regulatory Affairs
- Pharmaceutical Manufacturing
- Qualified Person Training
- Quality Management Systems
- Risk Management
- Senior Management
- Statistics
- Sterile Products
- Supply Chain and Distribution

Risk-Based Decision Making for Quality Professionals and QPs

March 2-3 | Manchester, UK

Course Fee: £1500 plus VAT

GMP for Biological and Biotechnology Products

March 8-11 | Manchester, UK

Course Fee: £2240 plus VAT

Quality Management Systems

March 14-18 | York, UK

Course Fee: £3350 plus VAT

Free QP Seminar for Prospective QPs & Sponsors

March 15 | York, UK

Course Fee: FREE

Pharmaceutical GMP

April 4-7 | Manchester, UK

Course Fee: £2240 plus VAT

Pharmaceutical Legislation Update

April 7 | Manchester, UK

Course Fee: £750 plus VAT

A-Z of Sterile Products Manufacture

April 18-21 | Manchester, UK

Course Fee: £2600 plus VAT

QP Practical Module

May 9-13 | Glasgow, UK

Course Fee: £3530 plus VAT

Pharmaceutical GMP Audits and Self-Inspections

A17638

(An IRCA Certified Pharmaceutical QMS Auditor/Lead Auditor Course)

May 16-20 | Manchester, UK

Course Fee: £2810 plus VAT

Data Integrity Defined

May 24 | Manchester, UK

Course Fee: £750 plus VAT

Data Integrity in QC Chemical Laboratories

May 25-26 | Manchester, UK

Course Fee: £1500 plus VAT

*Early Bird or Multiple Delegate discounts apply to some of our courses. Please visit our website, **www.nsf.org** for full details.*

For more information 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.

NSF Health Sciences Pharma Biotech Consulting

The right people. The right solution. The first time.™

Modern Process Validation

June 7-9 | Manchester, UK

Course Fee: £1950 plus VAT

Investigational Medicinal Products

June 13-16 | York, UK

Course Fee: £2680 plus VAT

Risk-Based Decision Making in Sterile Products Manufacture

June 20-22 | Manchester, UK

Course Fee: £1950 plus VAT

Rapid Change Control

June 30 – July 1 | Manchester, UK

Course Fee: £1500 plus VAT

The Role & Professional Duties of the Qualified Person

July 25-28 | York, UK

Course Fee: £2680 plus VAT

Active Pharmaceutical Ingredients

September 12-16 | Newcastle upon Tyne, UK

Course Fee: £2880 plus VAT

Human Error Prevention

September 14-16 | Manchester, UK

Course Fee: £1950 plus VAT

Pharmaceutical GMP Audits and Self-Inspections

(An IRCA Certified Pharmaceutical QMS Auditor/Lead Auditor Course)

A17638

September 19-23 | York, UK

Course Fee: £2810 plus VAT

Risk-Based Decision Making for Quality Professionals and QPs

September 27-28 | Manchester, UK

Course Fee: £1500 plus VAT

A full, up-to-date course listing is available online

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2016 marks our 30th year in the business of providing training to the pharmaceutical industry. We're proud to be part of NSF, with all the benefits we can bring to our customers through the expertise and professionalism of our colleagues across the globe.

Although you may be more familiar with one of our former names, our values and commitment remain the same.

Book your place at www.nsf.org/info/pharma-training

John Johnson, NSF Health Sciences Pharma Biotech Consulting Executive Director, responds to questions from the **Ask John** series.

Expert Corner

John Johnson (NSF Health Sciences Executive Director) recently received a particularly thought-provoking and highly challenging question from an industry colleague at our free GMP seminar in Frankfurt.

"What are going to be the trends in the pharma industry over the next 5-10 years?"

In a world where long-held values and current wisdom are challenged on a daily basis, where the world economy coalesces and then spins apart in response to technological breakthroughs or adverse global events, how can any of us really foresee how the industry may be perceived in the next decade? There are so many influences on our future, some that are welcome, some that are tragic, some inevitable and some difficult to predict.

But, what is definitely true is:

Anyone would agree that the choices and investments we make now will have a direct influence on our ability to survive and indeed thrive in both the tough times and good times ahead. Success is not a result of happenstance and businesses can't just focus on the results of the next month or next financial quarter. If businesses are going to shape their own future, they will need to do so much more than that. Stakeholders in a business value the enterprise not just by today's results but the likely results for the mid-term future. So what trends may influence the future and what are the best companies doing to equip themselves for the journey ahead?

Here are some key items to consider:

Five to Thrive

1. Firms are no longer competing with similar sized firms with similar cultures or methods – It is a world economy and each new organization from each emerging geography brings a new energy, new approaches, technical innovation and competitiveness. This global trend will continue and being able to continually **benchmark and adapt, learn and evolve** will only become more critical.

2. With 24-hour access to information and trends, being able to **identify the risk of a crisis** before it breaks could be the difference between survival and extinction. If you can foresee the challenges and adapt better than your competitors, you remain in the market and they may not.

3. Skills and experience are and will remain in short supply. Being able to retain your best staff and develop expertise through **internal training** is going to be key. When staff members are engaged in rewarding activities, given guidance and freedom to challenge the status quo and are provided fulfilling experiences in a blame-free environment, they tend to give their best and keep raising the bar. If a commitment to lifelong learning is not part of the company's DNA, it can sometimes seem that people with 20 years of experience perform as if they have one year of experience repeated 20 times over.

4. While always keeping an eye on the long term, being able to **seize an idea or make the right decision with immediacy** is going to be increasingly valuable. Communications will develop at warp speed and if your team takes days or weeks to take action, the action may take them! Clear, unambiguous communication methods, including modern, attractive and engaging education styles (transferable across cultures and geographies) will help you to make changes more rapidly and more accurately.

5. As technology and expectations become more complex, the trend toward specialization will continue. Being a generalist, a person who knows a little about a lot, may be perfect in a small organization or start-up company, but can be a real hindrance when something unusual or unpredictable occurs. Many firms can't maintain a large overhead of specialists; especially if their need is sporadic even though at times their help may be mission critical. In many firms, corporate centers are being trimmed and come the moment of need, specialist help is contracted into the team. Knowing who to deploy when and to what extent intervention can make the difference between recovery or regulatory action is critical. During these exceptional times, you need to know who to trust and who to turn to.

For further information in this field, please refer to my youtube clips on GMP remediation and case studies – just type in NSF John Johnson and there I am. Better still, email me at **johnjohnson@nsf.org** and let's arrange a coffee and a chat.

NSF Health Sciences Pharma Biotech Consulting

The right people. The right solution. The first time.™

Our 2016 Webinar Program

Following the outstanding success of our 2015 program, we are pleased to announce what's on offer for 2016. We asked you to suggest some topics and we've incorporated your ideas into our FREE webinar series for 2016:

March:

Warning Letters: Causes and Prevention

Every warning letter or equivalent is preventable. We believe it's better to spend $100,000 preventing such action than millions in painful remediation. Dial in for invaluable guidance.

Remediation the Right Way

We believe remediation following a tough inspection is an opportunity to emerge stronger and more confident. Find out how by applying our 3Cs approach.

April:

The Tyranny of Key Performance Indicators

Is your life consumed by KPIs? Want to know how to generate measures that work for you, not the other way around? We believe less is more. If you're suffering from death by measure, this could save your life.

May:

Living the Relaxed Lifestyle – How to Stop Firefighting

Fed up with stressful firefighting? We can help you move from crisis management to continuous improvement and a more relaxed lifestyle.

June:

Judgement Calls – Making Decisions Under Pressure

When the pressure is on, decisions are compromised by stress and emotion. This webinar will appeal to those who want to make good decisions in challenging situations.

September:

Struggling? Here is Your Survival Tool Kit

We asked 100 seasoned pharma professionals to share their tips on how to succeed and stay sane. Dial in to benefit from 1,000s of years of combined experience.

October:

Blame Culture – How to Prevent and Remove Blame Before It's Too Late

Companies with a blame culture will struggle to survive. Don't be one of them.

November:

Resiliency – How to Take the Hits and Bounce Back

In this unpredictable world, companies who can take the hits from unplanned events and bounce back stronger will prosper. Want to know how to become more resilient?

December:

How to Communicate With Senior Management… and Not Be Ignored

The title speaks for itself.

Each webinar will last for 30 minutes.

For more information, to register or to join our mailing list please visit our website at **www.nsf.org/info/pharma-webinars**

NSF Health Sciences Pharma Biotech Consulting

Europe:
The Georgian House, 22-24 West End, Kirkbymoorside, York, UK, YO62 6AF
T **+44 (0)1751 432999** F **+44 (0)1751 432450** E **pharmamail@nsf.org**

USA:
2001 Pennsylvania Ave, NW, Suite 950, Washington DC 20006, USA
T **+1 202-822-1850** F **+1 202-822-1859** E **USpharma@nsf.org**

www.nsf.org

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