SICK OF FIREFIGHTING?

LEARN HOW TO MOVE FROM REACTION TO PREVENTION – FOR THE GOOD OF YOUR HEALTH

by Martin Lush, John Johnson, Jim Morris, Mike Halliday, Andy Barnett, Maxine Fritz, Rachel Carmichael, George Toscano and Nicholas Markel

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. Move to PREVENTION:

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 you make a difference. 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

DOCUMENTATION ERRORS

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

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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

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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-

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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

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DEVIATION AND CAPA SYSTEMS

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 y our 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

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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

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INSPECTION RESPONSES

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:

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- 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 432 999**

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
- [ ] 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

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

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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

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LEADERSHIP

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

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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

ABOUT THE AUTHORS

Martin Lush has over 30 years' experience in the pharmaceutical and healthcare industry. He has held senior management positions in QA, manufacturing, QC and supply chain auditing and has conducted audits and education programs for many hundreds of companies in over 25 countries.

John Johnson is passionate about helping organizations foresee and overcome the barriers to sustainable long-term growth. He brings 28 years' experience across a range of companies in the pharmaceutical and healthcare industry. He has worked in small, medium and large pharma biotech companies across the product lifecycle for a wide range of dosage forms, holding senior operational and corporate-level experience in operations and quality assurance and leading multinational companies in many strategic projects.

Jim Morris has over 25 years of pharmaceutical management experience in both plant operations and corporate offices, working with Pfizer, Cilag AG and Mass Biologics in the U.S. and Europe. He has held positions as Deputy Director QA/QC and Regulatory Affairs while at Mass Biologics, Director of QA/QC for the Biologics business unit of Cilag AG and a number of quality assurance and manufacturing roles with Pfizer over a 16-year timeframe, culminating as the head of Quality Assurance for Pfizer in Latina, Italy.

ABOUT THE AUTHORS

Mike Halliday has extensive pharmaceutical manufacturing management and QA experience, gained over 20 years working for three major international pharmaceutical manufacturers. Before joining NSF in 2003, he was Associate Director, Global Audit and Compliance for Wyeth Europa. He was also previously a partner at David Begg Associates (DBA). Mike is eligible to act as a Qualified Person and is an honorary lecturer at the University of Strathclyde.

Andy Barnett has worked with clients in the pharmaceutical, medical device, biologic and biotechnology industries,for over 20 years, to develop quality assurance and regulatory strategies for compliance with U.S. FDA regulations. His particular expertise includes providing statistical support for process development, process characterization and optimization; assisting with remediation activities, especially corrective actions and process improvement; and providing training in root cause, corrective actions and statistical methods for process improvement.

Maxine Fritz has 25+ years of combined FDA, industry and consulting expertise and is responsible for overseeing the Pharma Biotech practice at NSF Health Sciences.

Rachel Carmichael has over 20 years' experience of pharmaceutical manufacture, control and quality management including nearly 11 years as a GMDP Inspector for the UK Competent Authority, the MHRA. This includes serving as the lead inspector representative within the MHRA for the transition from the Medicines Act to the Human Medicines Regulation, SI 2012 1916.

George Toscano has more than 20 years of experience helping companies in the global pharmaceutical, biologic and biotechnology markets develop and execute comprehensive quality systems solutions. He is a recognized data integrity expert and has conducted numerous audits and assessments to evaluate companies' systems.

Nicholas Markel has 25 years of experience in the biopharmaceutical field and 15 years of experience providing general and strategic consultation to domestic and foreign clients in the biotech, biologic and pharmaceutical industries assisting with manufacturing issues, development of quality systems and regulatory strategies. Mr. Markel's areas of expertise include techniques used in biopharmaceutical production for human use, review and development of quality systems, conducting cGMP compliance audits, deviation investigation, CAPA generation and implementation, oversight of manufacturing contractors and manufacturing activities, overall project management, commissioning of new and revised facilities, process validation, man-in-the-plant services to oversee operations and compliance.

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