

Journal

2019, Issue 43



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welcome

Welcome to the first Journal of 2019. Our theme this issue is **CHANGE** or suffer the consequences. You will find it interesting and provocative.

A few months ago, I attended a speed awareness course. In fairness this was long overdue – I have been ignoring my speedometer when driving on motorways for years. The course made me realize my stupidity and that it was only a matter of time before I injured myself or, worse still, someone else.

I had to change my speeding habit and used my understanding of behavioral change to do just that (follow the link to our **Changing Your Quality Culture and Improving GMP Behaviors** white paper at the bottom of page 5 to learn more).

Changing attitudes, behaviors (and driving habits) is possible, providing you are motivated and follow a disciplined process. It worked for me! Immerse yourself in Jim's **Managing Change** article on page 3, which examines different types of change and considerations for navigating each type. John's **Transformational Change** case studies (pages 6 to 9) show how we have supported clients on major change projects, one of whom wrote to us recently (see their comments on page 9).

We also provide the latest updates on industry rules and regulations (page 18) and then challenge the reason we need some of them (page 14)!

We hope you find this Journal useful. If there are any topics you would like covered this year, let us know.

Very best wishes for a prosperous 2019.



Martin Lush



Martin Lush,
Global Vice President, Pharma Biotech
and Medical Devices, NSF International



Managing Change

There is no time like the present...



by Jim Morris,
Executive Director,
Pharma Biotech,
NSF International

Organizational change can take on many guises. Most changes are planned and orchestrated by company management (such as a plant expansion, an updated MRP system or a new incentive program). However, some of the most impactful changes are nearly impossible to predict. Tectonic shifts such as Brexit leave lasting changes that play out over a long time. Changes can also result from a public health crisis (such as Heparin contamination and counterfeit Avastin). Adapting an operation to meet new regulatory requirements can be extremely demanding and costly, as with the work underway to implement serialization and the European Medicines Verification Organisation repositories. And unfortunately, some changes may result from a problem of our own making. For instance, a regulatory warning letter is usually preceded by a series of poor GMP inspections that point to reoccurring and often avoidable issues. Resolution of these issues will undoubtedly require significant changes to company quality systems and, in many cases, even larger changes to the company quality culture.

In all of these situations, change, regardless of its origins, always spells opportunity. What results is often an opportunity to improve what you do and what your company does. However, there are differences in the execution that will ultimately have an impact on how well a company, plant site or unit operation embraces change. Let's examine three types of change and considerations for navigating each type.

Change to Work

Planned changes of small or major design (such as a new method, new equipment or IT system) will typically be met with resistance. Company and personnel habits are strongly embedded, and it takes a lot of planning to overcome existing ways of doing business. Installing new manufacturing equipment or a new MRP system requires careful planning to ensure that personnel are competent in their environment before the system goes live. One of the most prevalent weaknesses in plant operations is a failure to gradually bring people on board with something different. As the adage goes, failing to plan is planning to fail. The operative word for any change to work is to PLAN to make the change in a way that involves the users early in the change process.





Change in Behaviors

Eliciting a change in behavior is truly the most challenging type of change to manage.

Examples of other behavioral-focused initiatives may include fostering a more safety-conscious culture across a plant network and developing a more positive donor experience among blood collection sites.

The driver could be a commitment made as a result of a serious problem (regulatory warning letter, product recall) or it could be a forward-thinking leader seeking to embed new behaviors that will help the company succeed in its mission. Consider leader initiatives such as Pfizer's CEO Ian Read promoting an "own it" philosophy across the company or ex-Alcoa CEO Paul O'Neill's focus on a safety-minded culture which dramatically improved operational performance and company valuation during his tenure as CEO¹. At NSF we have been asked to establish programs to create a more open and "speak up" quality culture across functional groups within multi-national organizations.

Regardless of the driver for change, companies seeking to embed a new behavior among all personnel need to carefully consider the following factors:

1. **The plan must come first.** A change that is only driven from the top is doomed to fail, whereas changes that enlist the buy-in from a broad cross-section of employees have the greatest chance of success. For instance, a biologics manufacturer seeking to foster a "speak up" culture across the organization leveraged first-line supervisor training sessions to cascade key messages and obtain broad-based feedback from employees. A large cross-section of employees were reached in this deployment and an appreciation for the behavioral changes expected was gained.

For a change to be successful, it must be taken on board by a critical threshold of like-minded people.

2. **Senior leadership must embrace the change and walk the talk.** There must be complete buy-in by the executive team for real behavior change to take place. If senior leaders express support for a change, but their actions do not, the initiative will not stand a chance of getting traction. For instance, if managers cancel safety meetings or put quality metric reviews last on a meeting agenda, they are indirectly communicating their lack of support. In contrast, if a safety meeting is never cancelled and quality metrics are first on the agenda, the message is clearly reinforced.

Senior leadership must be authentic in their expression of support.

3. **New habits must be reinforced.** A new habit is introduced through constant, visible reinforcement. The flavor of the month comes about when there is a lack of reinforcement and we move onto the next initiative. It is better to focus on getting a single initiative right than expecting employees to tackle multiple large-scale initiatives successfully. Does implementing a new MRP system, on top of the roll-out of a new LIMS system, while rolling out a cultural change initiative sound familiar?

Beware of the risk of initiative overload in a company or plant site. Recognize the value of a constantly reinforced simple message. It will ripple throughout the organization.

¹ C. Duhigg, The Power of Habit

4. **Success must be measured.** Change programs require the identification of indicators to measure impact and success. At NSF we work hard with each client interested in a change initiative to consider the measures needed to determine the impact of the program. Positive shifts in quality trend data is one approach or anecdotal measures of employee engagement may provide useful input. Measurement criteria must be part of an initiative and defined early in the change process.

If we don't measure it, we cannot gauge success.

Unexpected Changes

Often change comes about as a result of a surprise “gift” that lands on our doorstep. Experienced managers will recognize the opportunity and embrace it. For instance, I have used an example of a plant that was cited for cross-contamination risk of two highly sensitizing drug substances. This risk was escalated to the regulatory agency and resulted in a partial plant shutdown, remediation of the site quality systems and ultimately a series of regulatory agency re-inspections to confirm the cross-contamination risk had been eliminated. Twelve months later I must have looked twelve years older.


The salient message learned throughout the experience was the focus of the plant on one thing – the investigation report into the root cause of the cross-contamination. The depth of that report and resulting CAPAs saved the day (and the plant).

By focusing on the primary issue and not losing sight of its importance, the plant staff worked through a partial plant closure and began to make the changes to improve long-needed quality system improvements at the site. It was also critical to engage outside support – not only across the company plant network but external consultancy support. The “gift” wrapped in the unpleasantness of regulatory action, was the opportunity to make timely and lasting improvements to the site quality systems.

Conclusion

What is common in the above situations is the need to be tenaciously focused on the thing that you are seeking to change. Change is met with skepticism and resistance. People need to travel the journey from denial to commitment as quickly as possible and gain an appreciation for why the change matters. When change sponsors paint a picture of the future (what good looks like) and a critical threshold of people embrace the change, only then will that change begin to take shape and become embedded in the new way of working.

Denial No way, this is not my problem.	Commitment I am on board.
Resistance I don't have the time on top of everything else I am doing. This won't work.	Exploration I get it. Am beginning to understand. My peers are recognizing this is important.



Get more valuable guidance on changing GMP behaviors by applying our B = MATH model in the white paper *Changing Your Quality Culture and Improving GMP Behaviors: What Works and What Doesn't* available in our resource library, www.nsf.org/info/pblibrary.



by John Johnson,
Vice President,
Pharma Biotech,
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YOU MAY HAVE WON THE BATTLE, BUT HAVE YOU WON THE HEARTS AND MINDS?

John Johnson recounts an assignment where the easiest step to take was to change the SOPs and batch records, but would this alone lead to the business improvements that were so sorely needed?

Everyone thought they knew the source of the problem, yet no one had articulated what the problem actually was. Everyone was pointing a finger at someone else, but no one was looking close to home. Everyone had tried to fix the SOPs at some point, but nothing had really improved very much or for very long. Alternative ways of working, some undocumented, were in place just to avoid having to tackle the real issue.

THE PROBLEM WASN'T BETWEEN THE PAGES OF THE SOP, IT WAS BETWEEN THE EARS OF THE SUBJECT MATTER EXPERTS.

If transformational change was only about changing work instructions and barking out the new way of working, wouldn't change happen much quicker? But it doesn't, does it? In fact, more and more SOPs, more complexity and more written guidance, more emailed podium statements and more corporate guidelines have a tendency to confuse, frustrate and distract us from doing the **right thing at the right time, for the right reasons**. Autocratic, single-layer solutions rarely solve anything. Yet in the heat of battle, some firms still lose sight of what is truly important to make transformational change proportionate, risk-based, owned by the team and durable for the long term.

Our client knew that the batch record had grown incrementally over the past five years, having reached version 24 in no time at all! But all attempts to improve right first time, batch release lead times, operational performance and yields had failed at the first attempt. Why? Because they had not considered the single most influential and complex factor in the operation: **the team of workers who actually do the jobs each day!**

Once NSF was engaged, we set out to experience the production process ourselves through observing the shop floor, talking to staff who do the tasks and seeing the process from end to end. We watched the ridiculously complex nature of the processes the operators had to follow, the overly complex SOPs no one read, and the completion of the batch record sheets. The batch record, for a single shift operation, had over 90 pages and over 500 separate entries. We evaluated the tools the operators were given to use (largely ancient and in poor repair). We watched the techniques they were expected to perform (many irrelevant or fraught with error modes) and we evaluated some of the workarounds they had to do to get the job done (many of which were not prescribed in SOPs or recorded in GMP worksheets).

We also spoke to the team who was responsible for performing the work, asking questions, listening to the answers and asking for input. **We solved problems for them immediately and this rapidly built trust and credibility.**

Utilizing a range of techniques including voice of the customer and FMEA, over a three-week intensive period, we were able to propose (in full support of the line managers and with full input from the shop floor) a new batch record that stripped out as much complexity, error mode, transcription requirements, calculations and ambiguity as possible. This proposal reduced the number of pages by almost 60 percent to less than 35, and reduced documentation entries to less than 200 with 10 fewer transcriptions and no need to divide and reassemble the batch record. We utilized a regulatory compliance expert to tackle any



local concerns regarding the registration and to help manage the batch record upgrade project as a change with only minor regulatory impact. The new batch record was clearer on what is important (inventory, critical process parameters, second person checks and process monitoring) and stripped out everything that didn't add value to the quality and GMP compliance of the process and product.

But, did this alone have the desired effect?
If we had stopped there, the answer would be no.

What made all the difference?

- > We got staff at all levels talking to each other, **and listening to each other.**
- > We made it more natural for line managers to coach their team, explain their concerns openly and consult/act on the feedback from the shop floor.
- > We helped line managers engender a new level of engagement with the shop floor, helping everyone to see the value they bring to the organization and why they should speak up, listen and act for the benefit of the organization and ultimately for the patients they serve.
- > We performed specialist customized training in root cause analysis, human error reduction, simplification and cGMP so that the team was left with the skills and confidence to find other projects that needed their rigor and attention. We also coached people on how to speak to each other in a way that supports a blame-free culture.
- > Once the batch record was approved and in use, we came back and ran further checks to verify the change was

effective and durable. We provided solutions to areas of further concern and we helped the team form a habit; a simple habit to seek simplification in every change being contemplated.

The results speak for themselves:

- > Right first time in documentation increased from 65 to 94 percent.
- > The number of deviations per manufacturing process performed was reduced by 45 percent.
- > QA batch release lead time for batch review and approval was reduced by an average of three weeks.
- > On time in full and schedule adherence improved markedly, with costly inventory reductions made too.

But what made us especially proud? It is quite simple. We loved the fact that late finishes in the evening dropped 30 percent, meaning people left work on time more often than ever before. Why was that so important?

Again, it is very simple. What does your family remember most...

- > The elegance and complexity of a deviation investigation report you had to stay late to write again, or
- > The fact that you made it in time for your child's school play, their birthday dinner or your parents' anniversary celebration?

Focus on what is important and make changes that help your organization and your team, and most of all, that benefit you personally. This approach, and a focus on human behavior, is what really drives long-lasting change.



by John Johnson,
Vice President,
Pharma Biotech,
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Transformational Change Takes Time

Quick Fixes are Rarely Long Term Solutions

Back in 2014, we were approached by a relatively small company in Eastern Europe who had been referred to us by an established client.

GM Pharmaceuticals in Tbilisi, Georgia had an ambition to change itself from top to bottom and the goal was to raise standards across the Tbilisi facility, so that it could demonstrably meet WHO GMP guidelines and, at some later stage, meet EU cGMP expectations and host a GMP inspection from the European Medicines Agency. Why was this such a transformational change? At the time, there were literally no other major pharma manufacturing companies in the region and no local regulatory authority responsible for submissions, inspections and enforcement.

So, to make this dream a reality, what did they need?

Sometimes I find it easier to answer that question by turning the question on its head! What they didn't need:

- > A long list of known/unknown GMP deficiencies
- > People who would just tell them what to do
- > People who would just write the SOPs and GMP documents for them
- > People who would just say "it's impossible" or "it's easy" or other platitudes

What they needed was inspiration, collaboration, guidance, coaching, patience and a longer-term, supportive relationship.

Since then, over the course of nearly four years, we have been working with the team in Tbilisi at least three to four times per year and the wider team have supported the site through:

- > Training in:
 - Vendor quality assurance
 - Change control
 - Deviation management, root cause analysis and effective definition of CAPA

- Cleaning validation and decontamination strategies
- Facility design, commissioning, validation and ongoing monitoring
- Management of stability studies
- Investigation of suspected out-of-specification results
- Training and qualification of lab analysts

- > Coaching in the preparation for, execution of and follow-up during various client and regulatory inspections
- > Mentoring of six to 10 of the team's critical position holders; providing on-site and remote guidance on how to interpret the cGMP expectations and how to deploy the resources available to best effect
- > Assembly of registration documents, position papers, goal setting and site objectives, as well as review of training records, training content and methods of verifying the effectiveness of training
- > Support to increase yield and output, and minimize reworking

Being on call is crucial. Being available and responsive at short notice has been key too, as life has a way of throwing up surprises at short notice. Time is never our friend in business!

So where are we now?

- > The site has rationalized its product portfolio, reducing complexity and cross-contamination risks.
- > It has improved its laboratories, layouts and utilities guided by our SMEs.
- > It has refined and simplified its policies and SOPs, making compliance more assured without adding ambiguity and complexity.
- > It is now facing the future with more confidence, expertise and experience interpreting EU cGMP.
- > It passes GMP inspections with fewer surprises and fewer GMP concerns.

What did they say about us?

Our key contact, Eka Koplatadze, Quality Director, wrote to us recently:

"GM Pharmaceuticals has been cooperating with NSF and benefitting from its consultancy for several years. We have worked with nearly 10 consultants on different projects including technical as well as quality management system issues like upgrading of production, validation studies, stability studies, risk assessment training, mock inspections, etc.

I would like to emphasize that GM Pharmaceuticals makes active use of services, trainings, audits, etc. from leading European consultancies, which enables us to make certain conclusions.

There are two main things which distinguish NSF from the other consultancies. The first is their excellent reputation. Any leading company and any successful manager who has any weight in the pharmaceutical industry has used NSF's consultancy or training services. It is true for the biggest leading firms all over the world. Even mentioning working with NSF promotes warmth and happiness on people's faces. They immediately start recalling their experiences with the consultants who have delivered the training course for them.

The second thing is the fact that the number of staff members in the room is continuously increasing while working with NSF experts. Staff members start preparing for working with NSF consultants a long time earlier and every minute is planned and scheduled with them. After working with the consultants, the actual project work starts at the company, which is an indicator for the management to evaluate the consulting service.

In addition to being experts in their own fields and GMP, all the consultants are amazingly pleasant; all of them share the character of having an incredible work attitude. Besides, they distinguish themselves with their brilliant communication with representatives of other countries and other cultures.

We are lucky and happy to have had the chance of working with NSF in the development of projects for our company."

Someone once said there's more to GMP compliance than GMP; and though of course we "major" in GMP, we believe that our personal interactions, cultural awareness and long term relationships are what really make a difference.

Also see our webinar: **Using Behavioral GMP to Create Perpetual GMP Inspection Readiness.**





by Richard Kettlewell,
Consultant, NSF
International

Tech Talk



CONTINUED PROCESS VERIFICATION

In an earlier white paper, Continued/Ongoing Process Verification which can be found in NSF's resource library (www.nsf.org/info/pblibrary), Pete Gough introduced the regulatory expectations for Stage 3 of the process validation lifecycle. This article builds on that introduction and poses questions to pharmaceutical manufacturers as to how and why the concepts of Stage 3 could be built into pharmaceutical quality systems.

Arguably products and processes were always subject to development (process design), and since the advent of validation as a concept in the 1980s, we have always validated them – to a lesser or greater extent. So, Stages 1 and 2 of the lifecycle have always been around, as has Stage 3 – or at least the expectation for it and we have tested, reported, reviewed change and periodically reviewed product and process performance, haven't we?! The reality is that while we chose to believe that our annual or periodic review reports demonstrate the ongoing control and capability of processes, the brutal reality is that these reports are at best 12 months out of date, and any opportunity to leverage information about a batch manufactured 11 months ago evaporated as soon as the QC analyst recorded the batch as a pass!

The expectations have also been reinforced by the regulators:

- > The FDA process validation guidance states that *"The goal of the third validation stage is continual assurance that the process remains in a state of control (the validated state) during commercial manufacture. A system or systems for detecting unplanned departures from the process as designed is essential to accomplish this goal."*

- > The revised EU GMP Annex 15 states *"Manufacturers should monitor product quality to ensure that a state of control is maintained throughout the product lifecycle with the relevant process trends evaluated."*

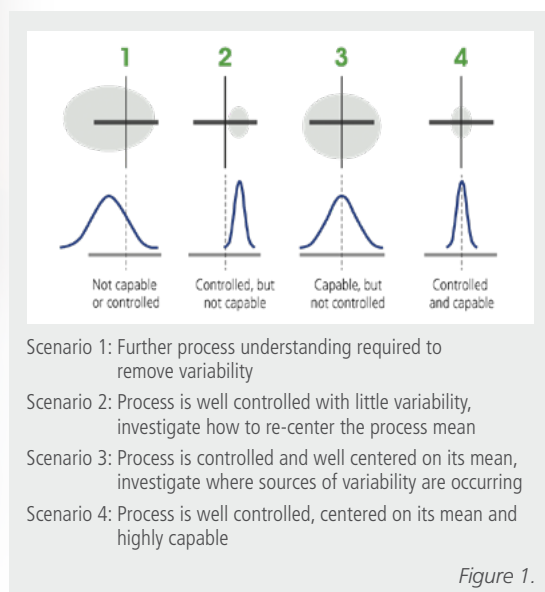
Perhaps the consideration here should be how the industry can take more from the requirement to do Stage 3, and consider it not a retrospective look back at performance, but a forward-looking predictive and anticipatory view of how continuous improvements can be made to established processes.

The expectation from the regulators then is reasonably clear – Stage 3 needs to be data driven and provide ongoing confirmation that the product/process of interest remains controlled and capable (see Figure 1). The first requirement **controlled** can be taken as a direct reference to the control strategy being employed:

- > How well do you understand what the patient/consumer needs (the quality target product profile, QTPP)
- > What is important in the product (the critical quality attributes, CQAs) and
- > What is important in the process that produces your product and its relationships to the CQAs (the critical process parameters, CPPs)?

But the control strategy is more than just measuring CQAs and controlling CPPs; importantly to the regulators there are other sources of variability in the process, the so-called material attributes.

The second requirement **capable** could reasonably be taken as a direct request to



calculate and monitor process capability, Ppk or Cpk, as indicators of how well a process is centered on its mean and, based on that, what capability the process has to produce consistently with minimal risk of producing defects.

The FDA is particularly interested in statistical evidence that the process remains controlled and capable, with sources of variability understood. For example:

Warning Letter 320-17-46 issued on Aug. 15, 2017 states “Your firm does not have an adequate ongoing program for monitoring process control to ensure stable manufacturing operations and consistent drug quality.” The response requested by FDA indicated that the manufacturer must “For each process, identify sources of variability in your raw materials and manufacturing process, and indicate the steps you have implemented to reduce variability or mitigate its potential effects on the quality of your products.”

The baseline for Stage 3 is clearly data and its timely analysis for underlying trends, shifts or excursions that could indicate that the process is in some way out of control or experiencing a variation either previously known or unknown. The value therefore is that Stage 3 offers the opportunity to react in a timely manner to prevent the potential loss of a batch or batches of product.

How often should the data be reviewed?

There is no single answer to this question, but the frequency of review should probably be

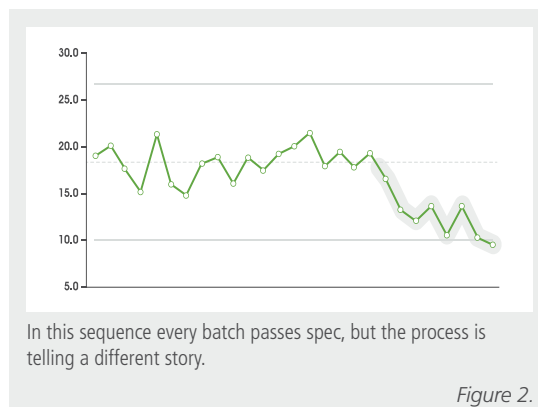
commensurate with the rate of manufacture. If a product is only made once every three months, monthly review is not commensurate. Likewise, if a high-volume product is made twenty times a week, there is sufficient new information to support a weekly review.

Who should undertake the review?

Again, no right or wrong answer, but it is important that **someone** does the review and that the business is aware of the output and motivated to take action when the product/process indicates it is in need of attention. Stage 3 provides the voice of the product – individual batches can only say **pass** or **fail**, but when you listen to an ongoing sequence of batch data, the message can be very different (see Figure 2).

When considering the who, it could be useful to consider RACI:

R	Responsible – for providing data, reviewing data, reporting data
A	Accountable – for it happening
C	Consulted – when things look abnormal
I	Informed – all ok, not ok



Can data review be used in a positive way to add value to other pharmaceutical quality processes?

The short answer is yes. A well-conducted and documented data trending program has the potential to make the periodic validation review process easier, help justify requalification/revalidation frequency and provide significant input to the periodic product review process. Where automated tools are used to extract data from site systems to facilitate trending, it is feasibly a small step to automate a large section of periodic/annual product reports.

With regards to change control, it's a regulatory expectation for effectiveness checks as part of the overall change management process. Data review can provide this post-implementation check and help illustrate that the desired change, (see Figure 3) or indeed no change, on process performance took place. How many validation exercises have been conducted in support of a supplier changing the site

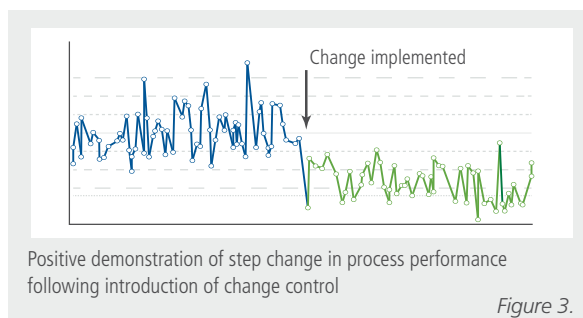


Figure 3.

of manufacture for a particular excipient, when the impact on the product is expected to be absolutely zero?! Could it be feasible to write the validation exercise in a different way to leverage the Stage 1 knowledge and Stage 3 data trending to illustrate the expected change or lack of change?

The data review process can be used to help illustrate process understanding. FDA places significant emphasis on understanding the manufacturing process and factors that contribute to variability to ensure a robust process validation exercise. The knock-on effect from lack of process understanding is potentially an unexpected number of out-of-specification events for which root cause cannot be determined, or an unexpected number of lot rejections.

Which attributes and parameters should I trend?

This comes down to product and process understanding, risk assessment and the question of available resources. The best answer is probably to trend everything, but clearly that is not practical in most cases. So, the answer is that risk assessment must be used so that those attributes and parameters that give indication of process change are most valuable for reviewing on a regular basis. For example, reviewing a set-point on a regular basis (e.g. adjust pH to 6.5) will most likely indicate a straight line on review and provide little information on the actual process. However, reviewing differential pressure across filter bags may correlate to the level of fines at discharge and ultimately impact product dissolution or compression performance. The value of Stage 1 manifests itself in Stage 3.

What limits should we apply?

For an established product with a large body of data there is the opportunity to derive statistically-based warning limits, but for new products it is most likely that trending against specification limits is the sensible approach, until sufficient data has been collected to permit further assessment to be made (see Figure 4).

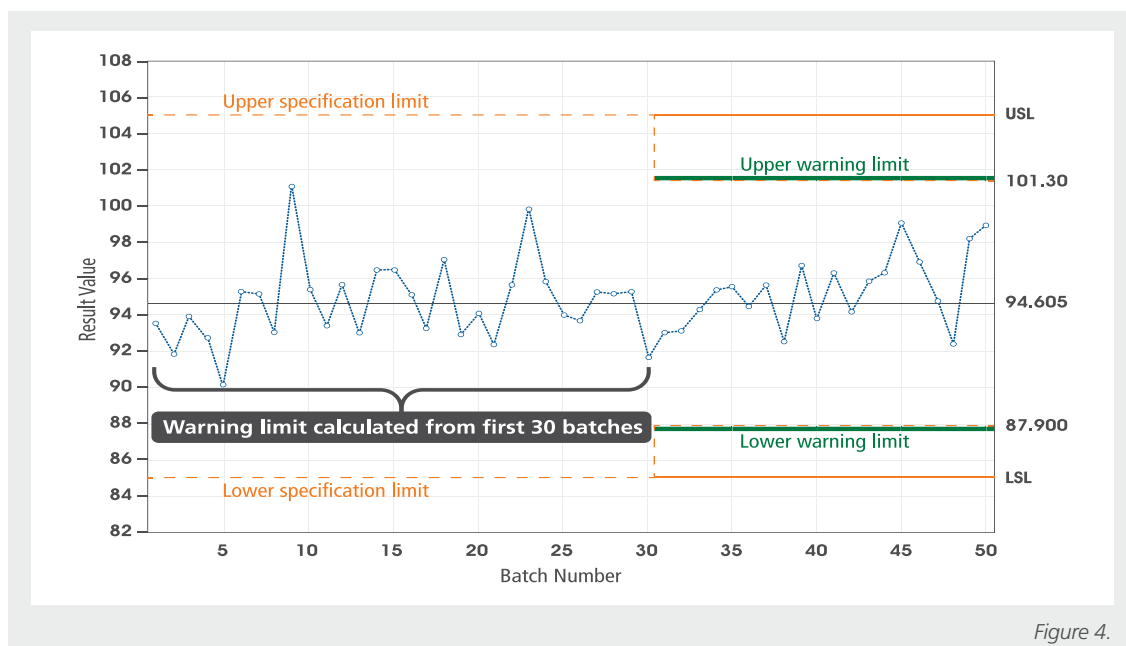


Figure 4.

If you have a question or need assistance then please contact us at pharmamail@nsf.org.

Countdown to European Medical Device Regulation

The implementation of the new European Medical Devices Regulation (MDR) and In Vitro Diagnostic Medical Devices Regulation (IVDR) has reached a critical momentum.

With only 20 months left in the transition period for MDR, medical device manufacturers that want to place medical devices on the EU market after May 26, 2020 are working diligently to implement the new regulatory requirements.

When it comes to budgeting and planning for additional regulatory resources, many manufacturers are still in gap analysis mode. The five hottest topics to meet compliance with MDR are:

- > Clinical investigation and evaluation
- > New roles and responsibilities for “economic operators”
- > Postmarket surveillance and vigilance, and market surveillance
- > Risk management and usability engineering/design input
- > Overhaul of labeling and technical documentation



by Oliver P. Christ, Executive Vice President, PROSYSTEM, an NSF International Company

Cost Drivers for MDR 2017/745-Compliant Technical Files

	Cost Driver Related to new requirements on	Effect on	# of MDR Articles Due to new requirements	Days of Work Estimated
1	Clinical	CER Update (~MedDev 2.7.1 Rev 4)	Evaluation § 61 Investigation §62-82	15-20 days
2	Risk Management	FMEA > Hazard/risk-based [Probability of occurrence of harm]	Annex I GSPR 1-9	5-10 days
3	Usability	No USE ERROR true commitment! [~ IEC 62366-1 + FDA guidance]	Annex I GSPR 5	5-10 days
4	Labeling	Consistency and validity of all labeling information (+ UDI)	Annex I GSPR 23	10-25 days
5	PMS	Living <u>all</u> feedback loops [Annual PMS and clinical follow-ups]	PMS §83 – 100	5-15+ days
6	Editorial Updates	Review of intended purpose Rewrite technical file contents	Annexes II + III	4-8+ days
On average ~2.5 month = ~50 days Premarket: 39-73+ days Postmarket: 5-15+ days				

The first notified bodies under MDR notification are expected to operate by the second quarter of 2019, one year prior to the end of the transition period. Compliance audits for MDR need to be prepared using ISO 13485:2016 as a basis for a compliant quality management system by adding in-depth processes required by MDR (e.g. for clinical investigation, postmarket surveillance, etc.). The new MDR Annexes II and III contain more detailed requirements for technical documentation for all classes of medical devices.

Now is the time to update “old” medical devices directive technical files to the new MDR requirements in Annex I (General Safety and Performance Requirements). The graphic above shows the estimated costs of implementing the new regulation. When companies do not have enough resources available in-house to do this job, external resources such as technical file development may be employed to manage the regulatory road map for success. Waiting is no longer an option. If you need assistance with this work, please contact ochrist@prosystem-nsf.com.



by Martin Lush,
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ARE NO RULES BETTER THAN BAD RULES?

*The Dangers of
Thoughtless
Compliance*

Like many of you I've been following the coroner's inquest into the tragic death of 15-year-old Natasha Ednan-Laperouse with interest.

For me it was personal. Both my children, like Natasha, have severe anaphylactic, life threatening food allergies. Natasha purchased a baguette from Pret a Manger (at Heathrow airport) and scrutinized the label for allergens. It's what every allergy sufferer habitually does... always check. Since sesame seeds (her anaphylactic trigger) weren't listed, she purchased and ate the baguette. Hours later she died from an allergic reaction.

The inquest exposed how Natasha had been let down by both law makers and Pret:

- > EU regulations state that sesame is one of 14 allergens consumers must be made aware of when used as a food ingredient.
- > However, EU regulations allow member states to decide how information about "non-pre-packaged food" (the baguette) is provided.
- > The UK's Food Regulation Agency allows "freshly handmade, non-pre-packaged food" to not be individually labeled. Why? To make life easier for food producers rather than protect allergy sufferers!
- > So, although Pret listed allergy warnings around its shops, packaging on individual products did not list allergen advice on the item, where allergy sufferers expect to find it. So, Pret was in compliance with the law. A bad law. They focused on meeting the rules, not the needs of allergic consumers making a potentially life-or-death decision on whether something is safe to eat?

To make this tragedy worse, Pret knew its practices were risky. There had been nine sesame-related allergic reactions in the previous year. Despite these warnings, Pret didn't act.

What Can We All Learn From This Tragedy?

- > Bad rules can be worse than no rules because those they seek to protect are lulled into a false sense of security. No sesame on the label means no sesame in the baguette, right?

- > Complex rules are bad rules. Rules **must** provide immediate clarity. Rules that meet complexity with complexity are worse than no rules at all. Complex rules lead to confusion, shortcuts and rule breaking. For rules to be effective, they must be simple.
- > Once written, rules are obsolete. The world has changed. To remain effective, rules must continue to evolve in light of new evidence, shifting objectives, changing conditions and real-life experience.
- > Rules that try to satisfy everyone are bad rules. Good rules focus only on who and what matters most.
- > Bad rules stifle the innovation we need to improve and grow. Remember, rules describe the minimum requirements. It's amazing how many companies include "to stay in regulatory compliance" in their mission statement. Aiming to comply with minimal requirements is hardly aspirational for an industry built on innovation and smart risk-taking.
- > Bad rules try to cover every eventuality. Good rules focus on the 20 percent that matters most.
- > Bad rules are written in isolation, without the participation of those who understand the situations in which they will be used. Our regulations would be so much better if patients and their advocate groups were sitting at the head of the rule-making table.

Pharma and med device companies have thousands of rules. From corporate and site policies to SOPs and work instructions and

everything in between. One company I recently visited had over 14,000 of them. Mostly bad, some dangerous. All were overcomplex and written without user involvement, and provided the dangerous illusion of control and order... when there was none.

Do You Have Good Rules or Bad Rules? How to Find Out

Ask as many of your colleagues as possible. Do we...

- > Apply a "less is more" approach to our rules? After all, smaller rules are simple rules and simple rules work.
- > Have a high trust environment that actively encourages people to challenge rules without fear?
- > Have confidence to challenge regulators when we're asked to comply with bad rules?
- > Have methods of trending failures to tell us the rule is not being followed or is just plain bad?
- > Use failures to encourage people to rip up the rule (even the whole book) and start again?
- > Make compliance easy? Pret's excuse (for not labeling products) was that allergy advice was posted in the shop. Next time you pass through Heathrow airport, go to Pret. It's noisy and crazy busy. Customers need simple, easy access to allergen advice. Listed on the product, not on a shelf meters away, obscured by other customers. Remember, if you want people to follow rules, you must keep them simple. If you don't, people take shortcuts.

- > Involve our patients and their advocate groups when we write our corporate policies?
- > Annually review how good our rules are based on performance and feedback?
- > Educate our people in the why (the rules matter) before the how (to follow)?

Questions for Our Regulators

- > When will you start writing rules with patient representation, because if you don't, how do you know they're fit for purpose?
- > When will you start reviewing rules that are no longer fit for purpose? For example, the rules governing post-approval changes discourage the improvements and innovation patients desperately need. This is a bad rule where everyone loses.
- > When will you change the rule-making process to keep up with the speed of science and technology? This must start sooner and involve all stakeholders including patients and their advocate groups.
- > Do we have too many rules? Has the (almost) exponential growth in number resulted in safer, better quality and more cost-effective medicines? Is it time for a mass culling?

I love the following quotes:

"There are no rules here. We're trying to accomplish something." Edison

"Rules are for obedience of fools and for the guidance of wise men." Day

Don't get me wrong, I'm not saying we don't need rules. We do, but we only need good ones.

Some Very Important Questions for You

Are your rules good or bad? Do they benefit the patient, or are they just a tick box exercise to satisfy the box checkers? Do you focus on meeting rules or meeting genuine needs of those who matter most?



Follow Martin on [LinkedIn](#) and get involved with the debate.



by Pete Gough,
Executive Director,
Pharma BioTech, NSF
International

Fragmentation of EU GMP – Not in Patients' Best Interest?

The original structure of EU GMP made perfect sense; Chapters 1 to 9 of EudraLex Volume 4 contained the baseline GMP expectations required for all medicinal products and the annexes contained additional, detailed GMPs for different types of product. In the past year the European Commission has moved away from this logical model by issuing completely different GMP requirements for different product types. This fragmentation of GMP has not been supported by industry and is being moved forward against the advice that the Commission has received from regulatory authority experts within the EU and the Pharmaceutical Inspection Convention/Cooperation Scheme (PIC/S).

ATMP GMP

In November 2017 the Commission issued GMP guidance for advanced therapy medicinal products (ATMPs) as a separate Part IV of EU GMP. This document duplicates many of the requirements in Chapters 1 to 8 of Part I and some of the annexes, but with some omissions; for instance, there is no mention of the need for self-inspections. The PIC/S had made strong recommendations to the Commission that this should be an additional annex to the existing GMP guideline and not a separate part.

IMP GMP

Annex 13 on the manufacture of investigational medicinal products (IMPs) is due to be replaced with a new IMP GMP document when Regulation 536/2014 is eventually implemented. The new GMP document was published in December 2017 and is currently available from the EudraLex Volume 4 web page underneath the current Annex 13. However, the new IMP GMP document is not titled Annex 13 so it is not clear whether this revised version will become the new Annex 13 when it is implemented or whether it will become yet another separate part of EU GMP.

If the current Commission's logic is followed for other dosage forms, we would have a ridiculous multitude of different GMPs for the many dosage forms that are currently covered by annexes, e.g. radio pharmaceuticals, medical gases, metered dose inhalers, etc.

Applicability of Annexes?

It appears that, unless specifically referenced in the separate parts, the provisions of the existing annexes do not apply to these new parts of EU GMP. For example, does Annex 1 on sterile products manufacture, which itself is undergoing a significant revision, apply to the manufacture of ATMPs (many of which are required to be sterile) and, if the IMP GMP becomes Part V, will it apply to the manufacture of sterile IMPs?

Drivers for Fragmentation?

The original concept of having the basic GMP requirements in Chapters 1 to 9 and the detail for the diverse range of dosage forms in the annexes was sound. It is unclear what has driven the Commission to abandon this model. Is it due to legal pedants narrowly interpreting new regulations? Is it due to lobbying by

interested parties to water down GMP for some sectors? Neither of these drivers are in patients' interests.

Part of the problem could be that new expectations, from legislation such as the falsified medicines Directive 2011/62/EU, which legally only apply to marketed human medicinal products, have been added to the Chapters in Part 1. This makes them also applicable to IMPs and veterinary medicines where there has not been any corresponding legislative changes. However, rather than introducing a multiplicity of new GMP parts, a more scientific response to this issue would be to revisit the contents of Chapters 1 to 9 of Part I to ensure that they truly only contain the baseline expectations for all products and, if necessary, introduce a new annex to cover the specific additional requirements for marketed human products.

Looked at in isolation, these separate GMP standards may appear to make sense. However, the added complexity for any organization making conventional medicines, ATMPs and IMPs will prove challenging as it is always difficult to maintain different

standards within the same organization. This fragmentation of GMP for medicinal products is introducing unnecessary complexity and confusion for organizations trying to provide safe, effective medicines for their patients, which cannot be in patients' best interests.

A Way Forward – EU and PIC/S to Diverge?

The PIC/S GMP guidance has historically been virtually identical to that of the EU. Given their initial opposition to issuing the ATMP guidance as a separate part, it is hoped that PIC/S will continue to be more logical and issue its ATMP guidance as an annex to the current Part 1 and retain the IMP guidance as Annex 13. Post-Brexit, I would urge the UK MHRA to take a leadership role within PIC/S and champion the retention of the original GMP structure, rather than adopt the new fragmented EU structure. If the European Commission wishes to make GMP more complex, it will be advantageous for the UK to retain the logic and simplicity of the original concept.



If you have a question on this article or need assistance, please don't hesitate to contact us at pharmamail@nsf.org.



by Pete Gough,
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& Andrew Papas,
Vice President of
Regulatory Affairs,
Pharma Biotech, NSF
International

Regulatory Update

EU News

Implementation of Safety Features

The requirement for all packs to have safety features (some form of tamper evidence feature and serialization) becomes effective on February 9, 2019.

In September 2018 the Irish regulatory authority, the HPRA, sent a letter to all marketing authorisation holders (MAHs) in the Republic of Ireland. This letter stated "In circumstances where packs that bear the safety features are released to the Irish market before the implementation date, the manufacturer or the MAH must ensure that the required data are uploaded to the European Medicines Verification Organisation (EMVO) repositories system before the 9 February 2019. If the data have not been uploaded this will lead to the generation of a significant number of alerts in the repository system when the packs are scanned at wholesaler and/or pharmacy level."

In late October 2018 the European Commission, the European Medicines Agency and the Heads of Medicines Agencies sent a joint letter to all stakeholders about the requirements for the implementation of safety features.

This letter reminds EU MAHs that:

"For already authorised products, the addition of safety features to packaging requires an update of the marketing authorisation dossier. This variation can be introduced at the same time as another variation in order to reduce costs.

MAHs must also sign contracts with the National Medicines Verification Organisations or NMVOs (who are responsible for setting up the national repositories) in the Member States where they market their products. This will enable them, or their manufacturers, to store the required data on the unique identifier in the repository system. It is essential that all concerned MAHs register with the NMVOs to avoid bottlenecks and secure market access. As part of their contract, MAHs are required to pay fees to the NMVOs.

Marketing authorisation holders must also connect (onboard) to the European Medicines Verification Organisation (EMVO). Onboarding to the EMVO allows the central upload of unique identifier data through the European hub and is subject to a one-off fee."

The letter also states that, to date, only half of MAHs have registered with their NMVOs and the EMVO.

The letter says that "Pharmacies will not be allowed to dispense medicines with safety features if they cannot verify and decommission unique identifiers and must allow enough time to prepare for 9 February 2019."

The letter ends by stating "It is important that all stakeholders act now to ensure compliance with the new rules whilst there is still sufficient time to prepare." Given that the February 9, 2019 is very near, it is somewhat doubtful that there is actually sufficient time unless these preparations are already well under way.

EU-USA Mutual Recognition Agreement

The schedule for implementing the EU-USA mutual recognition of inspection agreement (MRA) continues to be met. The FDA has now confirmed the capability of Belgium, Denmark, Estonia, Finland and Latvia. With the confirmation of Portugal in September this means that the commitment to confirm six more EU Member States by December 1, 2018 has been met.



This just leaves the remaining eight Member States to be confirmed by July 15, 2019.

ICH News

New Members and Management Committee Members

At the November 2018 meeting of the International Conference on Harmonisation (ICH) in Charlotte, NC, USA, the Iranian FDA was admitted as an observer. This means that ICH now consists of sixteen members and twenty-eight observers.

New ICH Quality Topics

At the ICH meeting in November 2018, the management committee approved the formation of two new quality expert working groups and identified two other topics that will start in mid-2019.

- > The new expert working groups will start immediately to:
 - Revise Q2 (R1) Analytical Validation and also to write a new Q14 guideline on analytical procedure development
 - Write a new Q13 Continuous Manufacturing guideline
- > The two topics to start in mid-2019:
 - M12 – Drug Interaction Studies
 - E20 – Adaptive Clinical Trials

US News

Generic Drugs Updates

The FDA continued its effort to promote bringing generics to the market. This included taking on the improper use of citizen petitions (CPs) as a manner to delay entry of generics to the market by the brand manufacturer. A revised guidance issued October 2, 2018 for 505(q) petitions outlines factors FDA will use to determine if a petition is submitted for the primary purpose of delaying the approval of a generic application. FDA could deny a petition, based on this determination, and would make this public through the citizen petition docket as an additional deterrent and refer these matters to the Federal Trade Commission as it concerns anticompetitive practices. The actual impact of this new guidance may be limited as CPs have rarely delayed entry of generics.

To further the development of complex transdermal and topical delivery (TDS) generics that face less competition, the FDA issued a number of guidances. The complexity of TDS stems from the requirement to deliver drug to skin consistently and over a specified time by ensuring consistent adherence of the product to the skin. In addition to the 25 TDS product-specific guidances, FDA issued two guidances on October 9, 2018, *Assessing Adhesion with Transdermal and Topical Delivery Systems for ANDAs*, and *Assessing the Irritation and Sensitization Potential of Transdermal and Topical Delivery Systems for ANDAs*, with recommendations on the design and conduct of studies to evaluate the adhesive performance and the *in vivo* skin irritation and sensitization potential of proposed generic TDS.

Lastly, FDA is seeking to use global tactics to promote generic development. It recently submitted a proposal to ICH to harmonize scientific and technical standards for generic drug development (e.g. dissolution methods).

Harmonization would be aimed at reducing the number of studies (e.g. BE studies) that are required to meet approval by allowing the same study to be used across regulatory authorities. Among FDA's longer-term goal of global approval of generic drugs, it is also considering the possibility of a common reference standard in generic drug development. ICH was set to review the FDA proposal in November 2018.

FOR THE LATEST BREXIT NEWS AND REGULATORY UPDATES AS THEY HAPPEN DOWNLOAD OUR APP

Please note that to keep our regulatory updates as current as possible, we will only be posting a summary of updates in the Journal.



NSF News...



NSF at CPhI Worldwide 2018

The NSF team was happy to meet many new and existing clients at CPhI Worldwide in Madrid, Spain on October 9-11, 2018. Uniting over 45,000 pharma professionals from around the globe, CPhI Worldwide brings together the world's most prominent pharma executives and suppliers for three days of collaboration, information dissemination and discussions that will help to define the future of the industry.



From Left to right: Martin Krainz, Heather Taylor, Ines Gomez, David Waddington, Lynne Byers and Catherine Kay at CPhI.

Lynne Byers, Executive Director, Pharma Biotech at NSF International, presented the session **Managing the Pharmaceutical Supply Chain** which drew lots of interest. Lynne's session covered how you can use recent legislation to identify and manage risks in complex supply chains, as well as API supply chains, the QP declaration, and the prominent issue of Brexit and its potential impact on supply chains. If you would like a copy of the presentation, get in touch with us at pharmamail@nsf.org.

Lynne also hosted a media breakfast that covered the potential impacts of Brexit which was well attended. She was also busy in a closed-door roundtable discussion with CEOs and members of executive leadership teams from across pharma to share ideas and discuss key challenges regarding policy, regulation, industry growth, new markets and global challenges.

Thank you to everyone who visited our stand at the event and got involved with our discussions.

PDA/FDA Joint Regulatory Conference in Washington, D.C.

NSF International has become a mainstay at the annual PDA/FDA Joint Regulatory Conference in Washington, D.C., held this year in late September. The theme, **Putting Patients First: Ensuring Innovation, Quality, Compliance and Supply in an Evolving Environment**, went hand in hand with our expertise. Over the three-day conference, many people visited our exhibitor booth, where our team spoke on hot-button items such as supply chain shortages, major regulatory changes in the pipeline, handling aging facilities, data integrity and how to perform an effective supplier quality audit.



In Times of Change, You Need to Change!

NSF taking center stage at the HRS Networking Event in Piccadilly, London

In October, John Johnson (VP, Pharma Biotech, NSF International) was delighted to be a guest speaker and panelist at the prestigious Hyper Recruitment Solutions (HRS) networking event, held at the Royal Society of Chemistry in London. The event, **Quality & Regulatory Considerations for UK Pharma/Biotech**, was invitation only and fully booked a month ahead of time.



As founder of HRS and in hosting the event, Ricky Martin (winner of BBC TV's *The Apprentice* series in 2012) was keen to assemble a delegation of senior pharma professionals from across the industry and allow guest speakers to present, interact and then field some tough questions from the floor.

Alongside Bob Clay (representing TOPRA) and Toby Underwood (Royal Society of Chemistry), John Johnson was delighted to contribute to

this important and insightful event, making connections and observations about risk management, the new pharma requirements expected to be in EU GMP Vol IV Annex 1 and a post-Brexit UK pharma industry.

With 120 people attending, representing a range of international pharma companies from across the disciplines of quality, regulatory and industrial operations, we expected lots of interest and questions from the floor, and the event certainly didn't disappoint.

One message that came out time and time again was that in times of change, staying as you are is rarely an option. Becoming entrenched in the past and looking back with rose-tinted glasses is rarely an effective strategy. When change happens, it's time to change! It is also true that creative pessimism can never be relied on when making key decisions and that always "fearing the worst and preparing for Armageddon" is rarely going to provide the competitive edge that the industry needs.

The panel discussion, chaired by chief interrogator Mike Soutar and with an appearance from Lord Sugar (both from BBC TV's *The Apprentice*), was both lively and highly entertaining.

If you would like a copy of John's presentation, contact us at pharmamail@nsf.org.



NSF Announces Strategic Collaboration With NIBRT

NSF is delighted to announce a strategic collaboration with NIBRT in Dublin, initially hosting a GMP symposium and the **GMP for Biological and Biotechnology Products**

course at its award-winning biotech production facility in Ireland. This will bring NSF's leading biotech course to a world-class training and bioprocessing plant, allowing attendees amazing access to the facilities, utilities and equipment associated with the common bioproduction methods. Course leader John Johnson said, *"This will help take the learning experience to another level and will enhance NSF's presence in this important biotech hub"*.

Forthcoming Courses & Workshops

What's Planned From March to May 2019

Pharmaceutical Formulation and Processing Part 2

March 11 – 15 | York, UK | Course Fee: £3,230



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

March 19 | Manchester, UK | Course Fee: £810



Regulatory Affairs for QA: Marketing Authorisations

March 20 | Manchester, UK | Course Fee: £710



Regulatory Affairs for QA: Variations

March 21 | Manchester, UK | Course Fee: £710



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

March 21 | Amsterdam, Netherlands | Course Fee: £810



Pharmaceutical GMP Audits and Self-Inspections

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

March 25 – 29 | Manchester, UK | Course Fee: £3,040

Pharmaceutical GMP – Presented in German

March 26 – 28 | Hamburg, Germany | Course Fee: €2,550



A-Z of Sterile Products Manufacture

April 1 – 5 | Manchester, UK | Course Fee: £3,170

Data Integrity – Presented in German

April 2 | Hamburg, Germany | Course Fee: €850



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

Pharma Biotech eLearning

Choose from NSF's range of pharma eLearning sessions including:

- > Computerised Systems Validation
- > GMP for Engineers
- > GxP Inspection Management Lifecycle
- > Human Error Prevention: Best Practices from Industry
- > Microbiology: The Basics
- > Pharmaceutical EU Legislation Update
- > Self-Inspections – How to Make Them Add Value to Your Organization
- > SOP Writing and Revision
- > The Roles and Responsibilities of an RP



New sessions are being added every month!

Visit www.nsf.org/info/pharma-e-learning for more information. We also offer medical devices eLearning – visit www.nsf.org/info/md-elearning for more information.

Human Error Prevention – Presented in German

April 3 – 4 | Hamburg, Germany | Course Fee: €1,700

**Introduction to Validation**

April 2 | York, UK | Course Fee: £710

**Cleaning Validation**

April 3 | York, UK | Course Fee: £710

**Pharmaceutical Quality Systems**April 8 – 11 | London, UK – *new location!* | Course Fee: £2,870**Auditing QC Laboratories**

April 30 – May 1 | Manchester, UK | Course Fee: £1,420

**Pharmaceutical Microbiology**

May 13 – 17 | York, UK | Course Fee: £3,230

**Free QP Seminar for Prospective QPs and Sponsors**

May 14 | York, UK | Course Fee: FREE

2019 Webinars

- | | | | |
|-----------------|---|------------------|---|
| FEBRUARY | > Disruptive Thinking and New Technologies in Pharma Manufacturing and Supply | JUNE | > Trends and Hot Topics in the Manufacture of Biotech Products |
| | > Pharmaceutical Operations – What Does the Regulator Expect to See During a GMP Inspection | JULY | > Introduction to the GMP Standard for OTC Drug Manufacture NSF/ ANSI 455-4 – 2018 |
| MARCH | > How to Install a Data Governance Process from Ground Zero | SEPTEMBER | > What do Regulators Check for When Auditing Cleaning and Cleaning Validation |
| APRIL | > SOP Simplification in Pharma Operations | OCTOBER | > The UK Qualified Person – Best Practice for Gaining Eligibility |
| | > How to Write a Contamination Control Strategy for Your Production Facility | NOVEMBER | > What are the Key Topics When Auditing a High-Speed Packaging Facility |
| MAY | > Managing Contract Qualified Persons – What Do You Need from Them, What Do They Need from You? | DECEMBER | > How to Resolve Conflict Within Multi-National Organizations so That Everyone Flourishes |

Keep checking www.nsf.org/info/pharma-webinars for further information.**MEET
OUR TEAM
AT...****2019 IPEC Europe Annual Excipients Forum** | January 31 | Malta, Europe**Making Pharmaceuticals UK** | April 30 – 1 May | Coventry, UK**FDLI Annual Conference** | May 3 – 4 | Washington, D.C., USA**Royal Pharmaceutical Society QP Symposium** | May 16 | London, UK**Key to Symbols:** Workshop QP course Presented in GermanFor 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.

Simplification and Improvement of a Change Control System



What we found

- > 56-page change control (CC) SOP that no one could understand. Even the process flows (there to simplify) caused brain freeze.
- > On average, change requests took 12–16 weeks to approve.
- > Because the system was so slow, there were various (some dangerous) workarounds and unofficial shortcuts.
- > The CC system approved everything.
- > Most approvals were based on gut feel.
- > The CC committee was made up of eight people who reviewed change requests remotely.

- > There was no follow-up of approved changes to measure success.
- > There was **no** control over routine changes.

What we left after NSF simplification

- > The SOP was reduced to seven pages.
- > Approval time was reduced from months to 60 minutes.
- > Workarounds and shortcuts became obsolete.
- > The CC system rejected between 38–40 percent of change requests (a good indicator of an effective CC system).
- > Customized impact assessment forms were introduced to make decisions objective and business focused.

Steps taken

- > Gap analysis of the CC system vs. best industry practice.
- > A two-day, distraction-free workshop with all key stakeholders delivered to 25 participants to simplify the SOP.
- > Core purpose of the CC system agreed upon with a focus on speed and importance of objective decision-making.
- > CC system and unofficial systems process mapped.
- > Non-value-adding steps removed.

- > Customized impact assessment forms generated.
- > Role of the CC changed from discussion to decision-making; CC members reduced to just three who met weekly (minimum).
- > Agenda of the CC clinic simplified.
- > All approved changes followed up to assess ROI.

Tools used

- > Gap analysis.
- > Process mapping.
- > Brutal thinking.
- > Risk assessment.
- > Customized impact assessment.

Return on investment

- > Everyone slept easier at night knowing they had, for the first time, control over routine changes.
- > Only changes delivering value were approved. This dramatically reduced initiative overload and freed up resources.

Behavior changed

People recognized that the CC system was vital to the health of their business and was not just about compliance.

Key message

Simplification motivates and inspires. People went from loathing (and ignoring) the CC system to loving and using it.



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