The Cost of Quality
Can We Really Afford to Ignore It?
What You Do Matters – A Reality Check

When we follow the same routine day in and day out, we are in danger of forgetting the importance of what we do and the medicines we make. A few weeks ago, I had a reality check.

My daughter has acute allergies to lots of things. Nuts in particular. In her 18 years, she has experienced five severe, life-threatening anaphylactic attacks where we’ve had to use her EpiPen for intramuscular administration of adrenalin to keep her airways open. Eight weeks ago she had her fifth and most recent attack. We had just left a restaurant where we had been given the usual reassurances about nut-free food and ingredients. On this occasion, they were unfounded and she started to show signs of an anaphylactic attack. Thankfully she knows how her body reacts and what to do. The feeling of nausea and itching made her immediately swallow some antihistamine tablets. As her symptoms worsened she resorted to her adrenalin inhaler that usually helps to keep her airways open...except on this occasion. She looked at me and said “Dad, call the paramedics and use the EpiPen. Now.” I could tell from her appearance she was getting worse and her breathing labored. As I prepared the auto eject syringe, my pharmaceutical mind started to consider what could go wrong. What would I do if there was insufficient adrenalin due to poor filling? What would I do if one of the 20 syringe components jammed because of poor quality components? This is what 32 years in the pharma industry can do to you!

As I applied pressure to the syringe, the reassuring click, as the syringe delivered the right dose, brought immediate relief to us both. After the paramedics gave her a clean bill of health, we headed home. She recovered in hours, whereas it took me weeks.

As with every edition of the Journal, we feel sure you will find every article very readable and informative in equal measure. However, I would like to set every reader a personal objective. Remind as many of your colleagues as possible, from the shop floor to the boardroom, about the importance of what they each do in manufacturing medicines that transform and, in some cases, save people’s lives. The job of leadership is to keep people focused on our primary objective: supplying patients with medicines that are safe and effective. After all, if you allow people to forget this, you really shouldn’t be in business.

Martin Lush

President,
NSF Health Sciences
Pharma Biotech

www.nsf.org
Quality Metrics, Part 2
What Gets Measured Gets Done

In the Spring 2014 Journal (http://bit.ly/112SmcM), we introduced the topic of quality metrics. Since then, interest has grown considerably so we thought an update on progress was timely.

What’s the Big Deal?
The push for quality metrics took a major step forward in July 2012, when the US Food and Drug Administration Safety and Innovation Act (FDASIA) was passed.

• Section 705 of FDASIA requires FDA to replace the periodic inspection frequency with a risk-based inspection schedule. Risk is assessed based on compliance history and the inherent risk of the drug being manufactured.

• Section 706 gives FDA authority to obtain certain records from a manufacturer in lieu of or in advance of an inspection. Essentially, any document that is discoverable during an on-site visit is subject to this regulation.

• FDASIA Section 711 drives revisions to cGMP regulations to improve oversight of the manufacturing process and improve the detection of emerging safety and quality signals.

ICH Q10 reaffirmed the combined position of industry and its regulators:

“Performance indicators that measure progress against quality objectives should be established, monitored, communicated regularly, and acted upon as appropriate as described in Section 4.1 (Management Review of the Pharmaceutical System).”

So, in summary, performance indicators should be chosen to monitor the effectiveness of the pharmaceutical quality system and can include processes such as corrective and preventive action (CAPA), deviations, complaints, audits and regulatory inspections.

• FDA is actively seeking input on how quality metrics could be used to support the risk-based inspection schedules. The incentive for manufacturers is to develop metrics that objectively and sufficiently indicate the safety of their products and the effectiveness of their quality systems.

• These metrics would be submitted periodically to FDA (probably once per year), perhaps as part of the Annual Product Review (APR). In return, the top performers can expect regulatory relief in the form of fewer on-site inspections and fewer Prior Approval Supplements.

• Work to develop consensus on quality metrics began in earnest at a joint FDA-
Tech Talk

Parenteral Drug Association (PDA) conference in December 2013, Russell Wesdyk of FDA’s Center for Drug Evaluation and Research (CDER) Office of Strategic Products (OSP) delivered the opening plenary session. He assured attendees that the Agency will not use these metrics as a “restaurant-style grade”

- FDA is in listening mode. What metrics will work? How do we define them? How should they be used? What algorithm will be used to stratify risk? Wesdyk stated that the Agency would like to see three broad categories of metrics:
  - Product quality – with focus on the patient
  - Site quality – focusing on manufacturing performance
  - Quality system effectiveness – focusing on the quality system inspection technique (QST) six-system model. The first two categories would be collected at the Agency and used to adjust the inspection schedule, and the third category would be evaluated during the periodic inspections

Break-out sessions and presentations at the FDA-PDA conference were quick to point out the challenges that must be addressed.

- Can we agree on definitions?
- How do we balance lagging indicators with predictive measures?
- How do we objectively evaluate risk across such a broad industry spectrum of manufacturing processes, drug types and patient indications?

The International Society for Pharmaceutical Engineering (ISPE) responded to this challenge by holding two well-attended public meetings and issuing a white paper in December 2013: “ISPE Proposals for FDA Quality Metrics Program”. You can obtain current information on the ISPE Quality Metrics Initiative on the ISPE website (www.ispe.org/quality-metrics-initiative). Manufacturers who participate in the ISPE Quality Metrics Pilot Program can influence the selection of metrics and definitions, obtain a blinded comparison data between companies and aseptic sites, and get a head start on metric implementation and data collection. As of October 28, 2014, 18 companies and 44 sites are participating in the pilot. If you would like to participate, contact PQLI@ispe.org.

What’s Next?
Based on FDA and industry input, ISPE has proposed 14 metrics and pilot company experience with these metrics will drive changes before the end of the year. The metrics are summarized in the table below.

Definitions for many of these metrics are available in the ISPE quality metrics white paper referenced above. Since life is far from perfect, we know that some of the proposed metrics will be difficult to measure, such as the CAPA effectiveness rate and quality culture. That said, articles in previous issues of the Journal could help.

Note! If you do not like the proposed metrics, here is your opportunity to get involved and influence the outcome!

Metrics that drive appropriate behaviors and actions by firms are needed. Deviation re-occurrence rates are clearly going to help companies focus on CAPA effectiveness. Furthermore, a metric that reduces reoccurring events and encourages straight-through processing will result in improved product quality.

Steven Mendivil, co-chair of the December FDA-PDA, provided some useful insights:

“Both the absolute value and trends of any given metric or suite of metrics might be valuable relative to making both direct comparisons (segmenting products and sites) and promoting continuous improvement.”

“Various factors make comparing raw metric data between companies very difficult. It isn’t only about the number (the metric) – it is about the trend and variability that measures risk and drives continuous improvement.”

Your Call to Action
1. ISPE has provided the opportunity to comment and influence – make use of it!
2. Move from data overload to becoming information savvy – start trending! Trend charts are the easiest way to detect emerging safety and quality signals, and can provide an early warning that quality systems or processes are unstable. Prompt action can prevent adverse trends from developing into higher reject rates and product shortages. Forward thinking companies are using trend analysis, evaluating process capability and using continuous process verification to their advantage as a tool to improve process reliability
3. Before selecting any measure, consider the behavior it will drive
4. Get the balance between leading (80%) and lagging (20%) indicators right
5. Less is more. Avoid ‘death by measure’ – the more you measure the less you know

Words of Wisdom
A pessimist sees the difficulty in every opportunity; an optimist sees the opportunity in every difficulty.

Winston Churchill
Some Personal Experiences

If prevention is 100 times cheaper than external failures, why isn’t management pushing for prevention? In a former role as a Division Quality Manager, I asked my engineers to invest at least 10 percent of their time on prevention activities. Just four hours every week. Frankly, I was tired of fighting fires and I was willing to let a few fires burn to prevent more fires in the future. This simple directive laid the foundation to support improvement and prevention activities, ultimately adding 8 percent to the bottom line in just three years. Not a bad return on investment.

In a recent situation, a client was experiencing periodic environmental excursions 10 to 20 times higher than the action limit for nonviable particulates. This had been going on for a long time. I created a trend chart from the data, pinpointed when the problem began and asked for the change log for that day. It turned out the HEPA filter was changed on the day the problem started. During an interview, the person responsible for the filter change mentioned he bent, by accident, a linkage on the filling equipment while making the change. It turned out that the linkage was rubbing and causing a high non-viable particulate count. Total analysis time – one hour. The savings in firefighting time and potential batch rejections? Probably more than $500,000. The trouble is this company, like many others, doesn’t bother to measure the cost of quality (COQ).

Cost of Quality: So How Is Our Industry Doing?

Jeffrey Macher, Associate Professor at Georgetown University, has some sobering statistics from an industry survey covering a range of dosage forms:

- Nearly 62 percent of respondents claimed that they do not calculate the cost of poor quality
- Ninety-two percent said they have not compared the cost of improvement with the cost of poor quality
- Twenty-eight percent estimated that a simple failure investigation costs over $10,000
- Sixty-five percent estimated that a complex failure investigation will cost over $100,000

The costs associated with regulatory sanctions (recalls, import bans, fines, disgorgements and lawsuits) were routinely $10,000s or $100s, respectively. Complaint investigations for failures identified prior to release to the customer, material review board (MRB) meetings and re-inspection of non-conforming materials, audits, calibration, validation studies and the materials and equipment used to complete these activities, are even more expensive. The costs of failure investigations were routinely over $1M.

Many of you liked our recent article “How to Talk to Senior Leaders in a Way They Can’t Ignore” (Issue 30 of the Journal, http://bit.ly/1ugvaU8). Frank Dollard, Associate Professor at Georgetown University, has some sobering statistics from an industry survey covering a range of dosage forms:

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- Ninety-two percent said they have not compared the cost of improvement with the cost of poor quality
- Twenty-eight percent estimated that a simple failure investigation costs over $10,000
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How to Estimate Quality Costs: The Basics

First, some definitions:

1. Prevention Costs: Include all prevention costs, such as training, product reviews, quality planning, improvement projects and the use of tools such as failure mode effects analysis (FMEAs), capability studies, process characterization studies, measurement studies, quality by design (QbD) and process analytical technology (PAT) initiatives, etc.

2. Appraisal Costs: Include incoming inspection, in-process and final inspection and testing, shelf-life stability studies, audits, calibration, validation studies and the materials and equipment used to complete these activities.

3. Internal Failures: Include scrap, rework and re-inspection of non-conforming materials, material review board (MRB) meetings and investigations for failures identified prior to release to the customer.

4. External Failures: Include failures detected by the customer including processing returns, customer complaints, recalls, lawsuits, adverse events and any rejected stock in response to a field incident.

To estimate each cost we have a simple choice. We can get very detailed or we can calculate a ballpark estimate as a function of total production costs or as a function of sales. For instance, capture your training costs both in terms of full-time equivalents (FTEs) dedicated to training and hours employees spend on training. To estimate prevention costs or time on proactive activities such as continuous improvement projects, conduct a poll asking engineers and managers how much time they spend on prevention-type activities. Then multiply the FTE by the average fully weighted salary. For most companies, this will be a relatively small number, probably less than 0.6 percent of COQ. It should be much higher. Even this simple example demonstrates one thing: If you invest in prevention, your total cost of quality will actually come down!

- For appraisal, start with the headcount for inspectors (assuming they are a separate function) or use a percentage if production workers spend a portion of their time in appraisal activities. Multiply the FTE by...
the fully loaded average labor cost. Use a similar estimate for maintenance personnel who calibrate and maintain automated and semi-automated inspection equipment. For pharmaceutical manufacturers, appraisal costs are higher than many other industries due to regulatory commitments, but these costs probably account for less than 25 percent of total COQ.

**For internal failures**, obtain the scrap rate as a percentage of production and apply this number to annual sales. In other words, 5 percent scrap is equal to 5 percent of annual sales. If scrap data is not readily available, take a random sample of batch records. Thirty batches should be sufficient for this initial estimate. Down the road, you can refine this estimate, since some products are more expensive than others. This approach will get you in the ballpark without investing in a new reporting system or counting every rejected vial, bag and label. Again, don’t get too granular and avoid the tendency to pursue too much detail in the initial stages — simply look at the big picture. Additionally, you should include labor for internal investigations; even simple investigations can cost thousands of dollars.

**For external failures**, estimate the headcount for conducting complaint/recall investigations and multiply by the typical weighted annual salary. Include the cost of returns, market withdrawals, recalls and a percentage of management costs for regulatory affairs, QC testing and management oversight. Once you have completed these initial estimates, add them up for the total cost of quality. It is important to state the amount in financial terms, rather than a percentage of sales or production quotas. In our experience, this initial estimate will probably understate the true cost. But at this stage, it is more important to gain awareness and establish a baseline. Senior leaders frankly switch off to compliance risks or risk of regulatory censure. In contrast, just imagine the impact these numbers would have. Leaders are far more likely to support improvement initiatives once they realize the magnitude of the opportunity.

### Struggling to get leadership support? Focus on taking the quality costing approach:

- **Start small** — don’t get bogged down in detail.
- **Focus first on eliminating failures**. Prioritize projects based on size of opportunity, likelihood of success and ease of implementation.
- **Although appraisal costs may represent a significant percentage of total COQ**, defer efforts to reduce these until achieving a substantial reduction in failure rates.

Over time, success will be measured by reduced internal and external failure rates, gradual reduction in appraisal costs and a greater percentage of the budget devoted to prevention.

Here at NSF we’re passionate about helping our clients succeed in a very tough climate. Decisions have to be fast and right. Quality costing, when done well, will prove to be invaluable. Please contact us if you have any questions on how to conduct and measure your COQ. We can also help support your process improvement and process optimization efforts.

If you have any questions or would like more information contact Andy Barnett at abarnett@nsf.org.
Regulatory Pathways of Drug-Device and Device-Drug Combination Products in the EU

So you have drug/device and device/drug combination products you want to get approved for the EU market? How do you go about this and how are these regulated? This article highlights how these products are defined in the EU market, what regulations apply and what agency authority is responsible for regulatory approvals.

Let’s first understand some simple definitions:

**Medicinal Product (MP)**
*Any substance or combination of substances which may be used in or administered to human beings either with 1) a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action or 2) to making a medicinal diagnosis.*

**Medical Device (MD)**
*Any instrument, apparatus, appliance, software, material or other article, whether used alone or in combination, intended by the manufacturer to be used for medical purposes for human beings, which does NOT achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means but which may be assisted in its function by such means.*
(Directive 93/42/EC)

### Comparison of MD vs MP

**Medical Device**
- Proportionality principle
- Technology-based
- Classified by risk
- Actions taken should be proportional to risks
- Primary intended purpose is achieved by physical or simple chemical means
- Large variety of products
- Inexpensive regulatory process

**Medicinal Product**
- Precautionary principle
- Science-based
- Primary intended purpose is achieved by physiological, metabolic or immunological means
- Limited number of products
- Expensive regulatory process

### Intended Primary Mode of Action (MoA)

In deciding whether a product falls under Directive 2001/83/EC (MP) or Directive 93/42/EC (MD), take account of the primary mode of action of the product.

### Examples

**Medical Devices**
- Wound dressing with antimicrobial agent
- Re-usable injector for use with insulin cartridge
- Separate application devices
- Heparin-coated catheters or stents
Medical Devices

Continued

**Medicinal Product**
- Wound treatment product for delivery of antimicrobial agent
- Disposable pen injector integral with insulin cartridge
- Needle-free injector containing medicinal product
- Heparin

**Combination Products**
- Medical product and medical device kit
  - In combinations which are classified as drugs; the device has, in most cases, a delivery function:
    - MP authorization by the competent authority (CA), application tool is MD (e.g. needle-free injector); if separate: CE mark required for the MD.
  - In combinations classified as devices, the MP has an ancillary function (must be proven): MD regulated by a notified body (NB), MP evaluated and approved via a consultation procedure with CA/EMA.

**Drug-Device Combinations I**
- Medicinal product has the primary action
  - CA/EMA evaluates the application dossier
  - Often administration devices only
  - Separate administration devices must be CE marked; additional data might be required (compatibility, functionality, toxicological data, etc.)

**Drug-Device Requirements**
- Clinical trial authorization
- Marketing authorization
- GMP manufacturer’s license
- Strict dossier format (common technical document (CTD))
- Demonstration of safety, quality and efficacy
- MD: data requirements of pharmaceutical directives and ER; CTD section 3.2.P.1, 3.2.R
- Variations need to be approved prior to implementation

**Device-Drug Combinations I**
- Main authority is the NB:
  - Monitor manufacturer’s (quality) system to produce declaration of conformity
  - Check if manufacturer follows the declared procedures and ER
  - Manufacturer has responsibility for safety and product liability (through declaration of conformity)
  - Device-drug combinations are usually Class III MD (highest risk)
  - Usefulness (clinical benefit/risk) of ancillary medicinal substance must be evident (NB report required for submission to CA); rationale/justification for using the MP in the device

**Drug-Device Combinations II**
- In case of blood products, EMA consultation is mandatory
- Contact EMA at least six months prior to procedure start
- Rapporteurs responsible for investigation and reporting to the EMA will be appointed
- Opinion is binding to NB; if an unfavorable opinion is given by EMA, the NB cannot issue a CE certificate
- Consultation is on quality, safety and usefulness (clinical risk/benefit) of the ancillary medicinal substance is required

**Consultation Procedure I**
- The NB shall seek a scientific opinion from one of the competent authorities designated by the Member States or the EMA on the quality and safety of the substance including the clinical benefit/risk profile of the incorporation of the substance into the device. (Essential Requirements 7.4)

**Consultation Procedure II**
- Consultation procedure between any NB and any competent authority in any EU member state
- Select NB with experience in combination devices
- Careful selection of the CA
- CA must complete evaluation and issue an opinion within 210 days upon receipt of a valid application
- The scientific opinion of the CA must be included in the documentation concerning the device

**Considerations for Device-Drug**
- Manufacturer is responsible for proper classification (case-by-case basis)
- MoA must be clearly stated and confirmed by sufficient scientific data
- Which legislation (MD vs MP) is applicable?
- Interpretation by NB and CA/EMA might differ
- Class III MD: full quality assurance and design examination – performed by the same NB

**Dossier Requirements**
- Technical File & Design Dossier for MD – evaluated by NB
- Consultation dossier for MP – evaluated by CA/EMA
- Risk analysis/evaluation/control
- Consider risk control for unacceptable hazards

**Clinical Investigation I**
- Regulatory pathway determines the clinical trial regulation
- Source of data: literature, clinical investigation or combination of both

**MD clinical investigation:**
- Completely new device (components, method of action unknown)
- Significant modification of an existing device which affects safety or performance
- New indication, purpose or function

**Clinical Investigation II**

**Medical Device**
- Annex X – Directive 93/42/EC
- MEDDEV 2.7/1 rev 3 Clinical evaluation: Guide for manufacturers and notified bodies
- National process
- No EUDRACT number required
- Evaluation by CA and EC
- No paediatric investigation plan (PIP) required; no legal representative in EU required

**Medicinal Product**
- Directive 2001/10/EC
- National process
- EUDRACT number required
- Evaluation by CA and EC
- PIP required (legally binding, compliance check prior to MAA); legal representative in EU required

**Outlook**
The Medical Device Directives are currently under revision. The European Commission proposed new rules on medical devices and issued a proposal for two regulations (MD and in vitro diagnostics MD) which should replace the current three directives. There are still some uncertainties about exactly what the new EU medical device regulations will contain and also when they will come into force in the EU. Unannounced inspections by your notified body and closer scrutiny of NB competence will certainly feature.

**Key Point Summary:**
1. It’s critical to understand the main mode of action of your product as that will determine whether it will be regulated as a medical device or as a medicinal product (drug) in the EU.
2. Once you know what regulation applies to your product in the EU, you need to understand what you have to do get your product approved and on the market.
3. If the product is regulated as a medical device, it will be a faster and less expensive process than that of a medicinal product (drug). If your medical device product contains a medicinal agent as a secondary function, it is likely to be regulated as a Class III device (high-risk).
4. You need to choose a notified body with the competence and experience in assessing combination products and also to select a CA with the appropriate competence and experience.
5. The developing new regulations of medical devices in the EU will have more force than the existing EU directives which are currently used.

In such a case, your notified body will have to consult with the competent authority (CA) about the safety, quality and usefulness of the medicinal agent in your product. As the CA is allowed 210 days after your submission to complete its evaluation and issue an opinion, this procedure is generally much slower than for lower-risk devices.

**Words of Wisdom**
If we want our regulators to do better, we have to embrace a simple idea: regulation isn’t an obstacle to thriving free markets; it’s a vital part of them.

James Surowiecki
Regulatory Update

EU News

EU GMP Chapter 5 (Production)
The final version of the revised Chapter 5, also dated August 13, 2014, was published in September. It contains the following changes:

- Sections 17 to 21 were updated to include a new section and to improve the guidance on prevention of cross-contamination and to refer to toxicological assessment
- Sections 27 to 30 were updated to include a new section on the qualification of suppliers in order to reflect the legal obligations introduced by Directive 2011/62/EU, the FMD and supply chain traceability
- Sections 35 and 36 were inserted to clarify and harmonize expectations of manufacturers regarding the testing of starting materials
- Section 71 introduces guidance on notification of restrictions in supply

Section 5.20 requires that “A Quality Risk Management process, which includes a potency and toxicological evaluation, should be used to assess and control the cross-contamination risks presented by the products manufactured.”

This section then states that the outcome of the quality risk management “should be the basis for determining the necessity for and extent to which premises and equipment should be dedicated to a particular product or product family.”

Section 5.21 provides a long list of technical and organizational measures that can be taken to mitigate the risk of cross-contamination.

In late November 2014 the CHMP/CVMP published the final version of the “Guideline on setting health based exposure limits for use in risk identification in the manufacture of different medicinal products in shared facilities.” This new guideline, effective from June 1, 2015, is to be used for the toxicological evaluation required by the revised Chapters 3 and 5 and the draft Annex 15 when conducting a risk assessment to determine the need for dedicated facilities and to determine cleaning validation limits in shared facilities.

The main features of the Chapter 5 changes relating to starting materials are a series of requirements to implement the legal changes in Directive 2011/62/EU, the Falsified Medicines Directive.

A new Section 71 has been added to provide guidance regarding “Product shortage due to manufacturing constraints”. This adds obligation for the marketing authorization (MA) holder to promptly notify the competent authority of “any constraints in manufacturing operations which may result in abnormal restriction in the supply.”

EU GMP Chapter 8 (Complaints and Product Recall)
The final version of the revised Chapter 8, dated August 13, 2014, was published in September along with the final versions of Chapters 3 and 5. All three revised chapters became effective on March 1, 2015.

This is a comprehensive change and the principal reasons for the changes are:

- To reflect quality risk management principles to be applied when investigating quality defects/complaints and when making decisions in relation to product recalls or other risk-mitigating actions
- To emphasize the need for the cause(s) of quality defects/complaints to be investigated and determined, and that appropriate preventative actions are put in place to guard against a recurrence of the issue
- To clarify expectations and responsibilities in relation to the reporting of quality defects to the supervisory authority

The new requirements include the following:

- The need for appropriately trained and experienced personnel to be responsible for managing complaint and quality defect investigations
- The need for sufficient personnel and resources to be available for the handling, reviewing and investigation of complaints and quality defects
- Central management of complaints that does not result in delays to the investigation and management of the issue
- A detailed list of items to be included in a quality defect investigation

There are new sections giving details of expectations for investigation and decision making and root cause analysis and corrective and preventative action.

In the recall section, the new requirements include:

- Any retrieval of product from the distribution network as a result of a quality defect should be regarded and managed as a recall
- For investigational medicinal products, all trial sites should be identified and the countries of destination should be indicated. The sponsor should implement a procedure for the rapid unblinding of blinded products, where this is necessary for a prompt recall
Regulatory Update

• It should also be considered whether the proposed recall action may affect different markets in different ways, and if this is the case, appropriate market-specific risk-reducing actions should be developed and discussed with the concerned competent authorities.

• The risk of shortage of an essential medicinal product which has no authorized alternative should be considered before deciding on a risk-reducing action such as a recall. Any decisions not to execute a risk-reducing action (eg a recall) which would otherwise be required should be agreed to with the competent authority in advance.

• Both within-office hour situations and out-of-office hour situations need to be considered when evaluating the effectiveness of recall arrangements and the need for mock recalls.

UK News

Guidance for UK IMP MIA Holders on the Use of UK Stand Alone Contract Laboratories

This guidance was issued in August 2014 and is applicable to all manufacturing/import authorization (MIA) holders manufacturing investigational medicinal products (IMPs) in the UK. It updates and changes the previous guidance published in June 2010. The guidance provides information on when a contract lab should, and should not, be named on an IMP manufacturer’s MIA. Most importantly, the guidance provides the MHRA’s expectations of the MIA holder’s responsibilities when using contract laboratories, which are:

• Have a system to assess the suitability, competency and GMP compliance of proposed contract laboratories prior to their use.

• Ensure that the contract laboratories used are visible within the manufacturer’s quality management system and listed in its site master file.

• Update their respective licenses/authorizations to name the contract laboratory if the contract laboratory meets the criteria for an MHRA GMP inspection.

• Ensure that a written technical agreement which describes the GMP responsibilities of each party, and also refers to the scope of testing and type of tests covered by the agreement, has been put in place.

• Have a system of ongoing supervision for contract laboratories, including arrangements to periodically formally reassess compliance, based on risk.

• Ensure that contract laboratories meeting the criteria for inspection have a valid GMP certificate prior to data generated by the laboratory being used by the contract giver for batch disposition decisions.

Note: The MHRA publishes a list of inspected stand-alone contract laboratories on its website. This list is updated at least annually.

Freight Consolidation Depots and Short-Term Storage of Medicinal Products

In August 2014, the MHRA published its position on freight consolidation depots (freight forwarders) and on short-term storage of ambient and refrigerated medicinal products in the Hot Topics section of its website. This position makes it clear that since the UK implementation of the Falsified Medicines Directive 2011/62/EU, both the act of export of a human medicine and the holding of a human medicine intended for export, by way of wholesale distribution, now requires authorization. This means that a number of companies and their sites that were not previously regulated now require a wholesale distribution authorization (WDA(H)).

The MHRA’s CQP Inspectorate is raising awareness of the impact of the UK regulations to those parties that are either directly or indirectly affected and any freight consolidator or freight forwarder in the air, sea or road transport sector that is either holding ambient medicinal products on site for more than 36 hours or has cold room facilities will require a wholesale distribution authorization WDA(H).

ICH News

ICH M7 – Genotoxic Impurities

At the June 2014 meeting, the guideline Assessment and Control of DND Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk received Step 4 approval.

This guideline offers guidance on analysis of structure activity relationships (SAR) for genotoxicity. Furthermore, it is intended to resolve questions such as whether impurities with similar alerts that potentially have similar mechanism of action should not be combined in calculating a threshold of toxicological concern (TTC) and whether the TTC may differ based on differences in the approved duration of use.

ICH Q12 – Product Lifecycle Management

A concept paper has been completed for a new guideline to address the technical and regulatory considerations for pharmaceutical product lifecycle management and was endorsed by the ICH Steering Committee on September 9, 2014. An EWG will start work on the topic at the ICH meeting in Lisbon in November 2014.

The proposed guideline will apply to pharmaceutical products, including currently marketed chemical, biotechnological and biological products. However, each regulatory authority will decide whether generic medicines can be included in the scope of this guideline.

This guideline is intended to work with ICH Q8 to Q11 Guidelines and will provide a framework to facilitate the management of post-approval chemistry, manufacturing and controls (CMC) changes in a more predictable and efficient manner across the product lifecycle. The specific change management issues that will be addressed by this guidance are proposed to be:

• The regulatory dossier:
  • Developing a harmonized approach to regulatory commitments
  • Delimiting the appropriate level of detail and information necessary for regulatory assessment and inspection in the dossier

• Quality system:
  • Establishing criteria for a harmonized risk-based change management system
  • Clarifying expectations and reinforcing the need to maintain a knowledge management system

• Post-approval change management plans and protocols
  • Introducing the concept of a post-approval management plan
  • Establishing criteria for post-approval change management protocols
  • Encouraging enhanced product development and control strategy approaches (QBD)

Adoption of this guideline will promote innovation and continual improvement, and strengthen quality assurance and reliable supply of product, including proactive planning of supply chain adjustments. It will allow regulators (assessors and inspectors) to better understand, and have more confidence and trust in, a firm’s pharmaceutical quality system (PQS) for management of post-approval CMC changes.
When Training Participants Spoke, We at NSF Health Sciences Listened

In April 2014, we contacted past, current and prospective NSF Health Sciences training course participants and asked them to respond to a brief online survey about their preferences and experiences regarding training. Who did they use for training and education services? If they have ever chosen NSF Health Sciences, why did they choose us? How did they measure the success of a training session? What was their preferred mode of training? Did they prefer training onsite at their worksite or traveling to a training location? These were just some of the questions we asked.

A total of 145 training participants responded to our email and LinkedIn survey requests. We originally thought the survey would help us plan, manage and market our training programs more effectively at NSF Health Sciences, but we soon realized the results were meaningful in other ways as well.

For instance, what was the average age of survey respondents? The vast majority (78 percent) were between 31 and 50 years old. Only 16 percent were over age 50. And only 6 percent were under 30. How do we interpret this data? The low number of participants under age 30 may be linked to career progression and experience.

Perhaps very few young professionals in the pharmaceutical industry are invited to attend company-paid, external training events. Their positions and job experiences may limit them to internal training opportunities. But what about those age 51 and older? Does their low rate of online survey participation suggest that people of that age need less training of the type that NSF Health Sciences provides to help them perform their current roles or to enhance and advance their careers? Or does the low participation rate simply indicate a lower tolerance for online survey solicitations?

The information uncovered by the online survey was certainly useful to NSF Health Sciences training developers and marketers, but it also has the potential to reveal many unexpected opportunities for our clients.

How Do You Prefer Your Training?

When asked how they prefer to attend pharmaceutical training courses, 75 percent said they preferred “external, public courses”. Of the remaining respondents, 17 percent said they like “in-house course delivered by external expert,” 4 percent said they prefer “webinars” and 3 percent said they prefer “e-learning courses.” One percent selected “other.”

What does this tell us about our customers’ preferences for training opportunities? The most important message is that, despite the fact that many training companies – and customer companies – are now promoting webinars, e-learning and desk-based learning packages as the future of “lifelong learning”, the vast majority of people receiving the education prefer face-to-face training courses. Comments indicate that a real, live tutor, via an external, public course provides a better, more effective learning experience, as well as a rare and valuable opportunity to interact with peers from other companies, to share common challenges and experiences and explore networking opportunities.

As one survey respondent said, “I believe nothing replaces face-to-face training, but what is equally important is the discussions generated during the training by various participants. I believe this would not be of the same quality and content if it were a webinar and we’d lose the networking opportunities which allow us to form relationships amongst various experts in other companies. I find this invaluable.”

Clearly, getting away from the day-to-day work environment and its demands – and meeting new people without your office mates and superiors looking over your shoulder – is a valuable part of the “external, public course” experience.

Some participants (17 percent) prefer an “in-house course delivered by external experts” due to the ability to customize content for a particular group. One survey respondent noted, “It is easier to tailor requirements to the needs of the attendees and it is often more efficient in terms of both time and cost.”

We agree with this point of view, which is why we put great emphasis on offering all our public courses as in-house events, where we work with clients to ensure they get exactly the course they want when they want it.

Only 7 percent of survey respondents prefer “webinars” and “e-learning courses”. They cited lower costs and flexibility as the main reasons. One survey respondent wrote, “E-learning is good because you can do it whenever you want. There is a lot of flexibility and follow up via email correspondence to tutor.”

Another said, webinars and e-learning are “…usually cheaper, and less travel, therefore easier to attend.”

So, despite the growth in electronic means of conveying learning, a massive 93 percent of respondents to our survey said that they prefer face-to-face training. This validates what we believe and we suggest that those in charge of learning and development at pharmaceutical firms keep this in mind when deciding on what training modalities to adopt to fully engage their employees in training and education.

Interpreting Online Survey Results

What Method Do You Prefer To Attend Pharmaceutical Training Courses?

What Is Your Age?

<table>
<thead>
<tr>
<th>Age</th>
<th>% of respondents</th>
</tr>
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<tbody>
<tr>
<td>21-30</td>
<td>6%</td>
</tr>
<tr>
<td>31-40</td>
<td>40%</td>
</tr>
<tr>
<td>41-50</td>
<td>38%</td>
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<tr>
<td>51+</td>
<td>16%</td>
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www.nsf.org www.nsf.org
Whom Do You Trust?

According to the survey data, 76 percent of respondents have used up to three training suppliers in the past five years. Most people had experienced two or three training providers. Respondents were asked to select up to five training companies they’ve used most frequently in the last five years. More than 80 different training providers were mentioned in the survey, but NSF was the clear leader with mentions by 69 percent of respondents. The next most popular training provider was mentioned by only 21 percent of respondents.

Trainer expertise and course content were most frequently mentioned reasons for choosing NSF over other training providers. Company reputation and quality of training were also frequently mentioned. One respondent wrote, “I have always liked the fact that NSF has active participation during the course by having lots of discussion, exercises and group work. The teachers/presenters have a lot of experience and knowledge about the industry.”

Another respondent summed up the NSF training experience like this. “They are the best and deliver the easiest material to learn from and train you to the right level of detail.”

This is very reassuring to hear and it makes all the hard work we put into our courses worthwhile.

So What Have We Learned From You?

We have learned many lessons from this survey. Perhaps for us (and for you too?) the most important messages are...

• Despite the growth in webinars, e-learning and other “modern” forms of education, the vast majority of you prefer traditional, face-to-face training from real, live tutors

• You put immense value on being able to meet with your peers from other companies and to learn from each other

• While duration of training courses, timing, location and cost can influence your choice of training provider, nothing is more important to you than the quality of the training and the trainers.

We are delighted to find that your views coincide exactly with our own and these messages will help to shape our strategy for education in the future. We believe that education plays a key part in maximizing the contribution of all people at all levels within the pharmaceutical industry and is essential to establishing a strong and sustainable quality culture in our industry. We will continue to embrace new and emerging technologies where they help us to reach people that we might not otherwise be able to reach and to enhance the quality of the learning experience for our customers, but we will not lose sight of what matters most – the effectiveness of the training and the enjoyment factor for the participant.

If you participated in this survey, we would like to offer our very sincere thanks. Your thoughts and recommendations have been immensely valuable to us. If you did not participate in the survey, we hope that you found this article informative and thought-provoking.
Congratulations to Bob Wherry

Congratulations, Bob Wherry! We are very pleased to recognize Bob for his accomplishments as a participant in the Quality Leadership Program and this year’s recipient of the QP Alumni Award for Outstanding Achievement. This award is granted annually by the NSF QP alumni group to a participant who demonstrated consistently high standards of work and an excellent high quality thesis. The award is granted on the recommendation of the University of Strathclyde following a review of the academic achievements of delegates on UK and US programs.

This award recognizes Bob’s broad knowledge of the pharmaceutical industry and specific knowledge of CSV. Bob’s thesis is The Application of ICH Principles to Computer System Validation. As QPs and delegates on the US program will attest, this achievement does not come easily! Two years of demanding course work, 12 rigorous week-long modules and a demanding thesis for those pursuing the MSc in Pharmaceutical Quality and Good Manufacturing Practice.

Bob will say his experience with NSF truly surpasses many of the educational programs he has experienced in his past. Bob holds a BS in Chemical Engineering from Lehigh University and an MS in Regulatory Affairs from Northeastern University. He is a current member of the ISPE GAMP Americas Committee and of the ISPE Boston Area Chapter Educational Programs Committee.

We wish Bob the very best in his endeavors as a consultant and active participant in the industry.

A Very Warm Welcome to Richard Funnell

We are delighted to announce that Richard Funnell joined our team of consultants in October 2014. Richard spent the past 11 years at the MHRA, most recently having reached the level of senior inspector, and has acted as an expert in IMP standards including representing the MHRA on a European level regarding the new Clinical Trial Regulation 536/2014. He has a special interest in sterile product manufacture and filling.

There is a long history of support at NSF from ex-MHRA inspectors. David Begg, founder of David Begg Associates (later to become DBA, NSF-DBA and now NSF) was a former senior inspector at the agency. David was followed by other well known and highly respected ex-inspectors over the years, including Peter Smith, Peter Monger, Liz Allanson (former head of the GMP inspectorate), Martyn Becker and Darren Jones.

NSF and its clients have benefitted from this wealth of experience and expertise bringing practical pragmatic solutions and advice. Many attendees of courses such as GMP, Audits & Self-Inspections, GMP for Clinical Trials and a good number of our QP modules have benefitted from the education, experience and fun that they have brought to the training room.

We’re confident that Richard will continue this fantastic legacy.
The QP Journey Continues

At the time of writing, I am reflecting on series 12 of our QP training and looking forward to the start of series 13.

We have had a fantastic series 12 (late 2012 to mid 2014) with increasing delegate numbers on modules enabling us to run certain modules in new locations, reaching an even wider European audience. Feedback on course quality from delegates reflects continued improvement and course development for what is already described by our delegates as the “gold standard” in Qualified Person training.

Our delegates share this success, with 22 new QPs passing vivas or assessments in series 12. We have enjoyed receiving phone calls and emails from some very excited individuals. Personally, I find the comments thanking NSF, the University of Strathclyde team, Stella (our QP administrator), their personal tutor or the tutors who put them through the tough revision interview particularly gratifying. It’s the sort of feedback that makes my role as QP course manager particularly rewarding.

Congratulations and best wishes to all those who worked so hard or who are working hard for their big day. The QP alumni continues to grow with students, newly qualified QPs and the experienced QPs turning up in ever increasing numbers to meet, agree on best practices, interact with guest speakers and meet the MHRA. This annual special event restricted to students taking four or more modules from our flexible QP training program is due, in no small way, to Mike Halliday, our Executive Director at NSF Health Sciences Pharma Biotech, leads on this “gold standard” of training offerings and if you have attended one of our QP modules – either as a potential QP, or to progress as a technical manager – you will no doubt be well acquainted with him. Here, Mike keeps you up-to-date with what’s happening in the world of the NSF QP.

With extensive experience in international QA auditing of a wide range of pharma manufacturers and specialist distributors, Mike is also a recognized expert in Auditing – a man of many talents! As such, Mike is the person responsible for our IRCA certified auditor courses. In Pharmaceutical (Certified) Auditor Education Mike reveals some exciting developments taking place with this popular course and provides five key points to keep you heading in the right direction.

Any questions on this “gold standard” of training offerings? Contact Mike at mikehalliday@nsf.org

Call to Action: 5 Key Points

1. Recognize that a robust and effective audit program is not just a legal requirement, but vital to your success
2. Remember that any audit is only as good as the auditor responsible
3. If you want confidence in your auditing programs, send your auditors on our unique and independently certified pharmaceutical auditor program. This will provide them with what they need to do a challenging job
4. Gain proof of competency through our course. More and more regulatory agencies are asking for this for key roles like auditing
5. Watch out for our certified internal auditing program, our CPD webinars and our new LinkedIn account, all designed to help you get the most from your auditing program

Don’t Get Left Behind

Our independently certified auditor education course has grown exponentially since its introduction in 2011 and by the end of 2014, we will have trained over 500 auditors seeking certification with IRCA (the International Register of Certificated Auditors, IRCA, is the leading professional body for management system auditors) as a Pharmaceutical Quality Management System Auditor/Lead Auditor.

Training has included self-out public courses and in-house courses for companies ranging from some of the largest multinationals to some of the smallest, each with the same objectives:

• To have a team of highly skilled and very competent auditors who practice best-in-class auditing principles and practices
• To have confidence in their auditing programs so vital in driving continuous improvement, reducing business risk and protecting their reputation and legacy

Several companies are now making attendance in this course a prerequisite for new recruits to their audit teams and also for their experienced auditors. We are also seeing increasing numbers of self-employed consultants joining the course to support their contract auditing roles. No wonder our own team of contract auditors goes through the course too!

Exciting New Developments

• Attendees will be invited to the first of regular CPD webinars on legal updates for auditors as a unique follow-up service
• We will soon be launching an additional LinkedIn discussion group to support and share knowledge and views. We want to help you in your development and help you to help others
• We will also be launching a Certified Internal Auditor course. We have already done this for a number of our clients keen to improve their vitally important internal auditing program. As you know, having a strong and robust internal auditing program is an EU legal requirement and so vital to managing risk

Words of Wisdom

Excellence is an art won by training and habitation.

Aristotle
Managing change effectively has a critical influence on being able to install and operate a lean quality system. Regrettably, it is very common for firms to miss the key steps that lead to selecting, empowering and trusting their team to properly triage change and, therefore, risk. Unsurprisingly, the team then has problems defining and executing tasks systematically so that changes are properly defined, justified and documented. “A common pitfall,” says John, “is to engage people in the team then has problems defining and executing tasks systematically so that changes are properly defined, justified and documented. “A common pitfall,” says John, “is to engage people in the culture of GMP, where fully documented, comprehensive documentation results in efficient and effective systems. This is justifiable and that the rationale for the required changes is documented thoroughly.

A related second question was:

“Our company grew very quickly without modifying the quality system to suit the new challenges and a year down the line we have suffered some bad feedback from GMP inspections performed by key clients and a regulatory agency. Key people have left and we are struggling to adapt. What would be a recommended next step for us?”

In times of rapid change, it is common for firms to focus on the top and bottom lines, not the systems that manage the business. GMP issues can surface very quickly if inadequate focus is given to the quality system. In one medium-size enterprise known to me, this deterioration took place over 18 months.

Maintaining GMP compliance is not a series of rests and sprints, it is a constant steady journey. Performance of the quality system is not assured by cycles of fulls and remediation. A sustainable cadence of risk detection, assessment and steady planned improvement will always prove to be better at delivering a long-term, sustainable business.

At the heart of this issue lies an inability to perform quality planning and then to execute the improvements ahead of time. Having a risk register drive the annual objective setting process (ahead of budget setting) ensures the company “fixes the roof before it starts raining.” In this case where GMP deficiencies have already taken hold, it is vital to:

• Engage the local team to deeply understand the issues and then take ownership for fixing them including appointing single points of accountability for the key CAPAs to be taken.
• Get a second view on the priorities and the feasibility of the capability of the organization to deliver the changes needed.
• Ally the CAPA plan with a detailed, interactive program of education for the critical position holders so that they can learn and debate the issues, and therefore foresee and take action the next time a crunch may occur.

Market research suggests that GMP remediation can be four to 10 times more expensive than a focused risk mitigation program and rarely, unless meticulously designed, drives a long-term sustainable approach to quality.
Struggling Day to Day? Here is Your Survival Tool Kit

I was with a client the other week helping them manage the outcome of a tough audit. While sat in the room late one evening, two things struck me; how tired and stressed they all looked and their relative inexperience. Their average age was 35, although some looked considerably older! Over a coffee, it was clear they were very committed and hardworking and wanted to do their best; they just didn’t know how.

Two years earlier their company encouraged those over the age of 50 to leave, who took thousands of years of priceless intellectual property with them. In short, those that remained had no-one to go to for guidance, advice, mentorship and support.

On returning to the office I contacted 30 people whom I have known and respected for many years. High calibre “streetwise” professionals with an average of 30-35 years’ pharmac experience, most of whom went through our Qualified Person education program. Like a lot of our QPs, they now hold senior leadership positions in their respective companies. I asked them the following question:

“What single piece of advice would you give the young and aspiring pharma professional that would help them survive and prosper?”

Here are their recommendations based on nearly 1,000 years of combined experience. Read carefully, there are some real gems!

In no order of priority:

1. When you’re in the middle of a crisis or you’ve made a final decision, ask yourself if your actions and decisions will pass the “headline test”. What would the newspapers say about it? How would headlines sound? What would you say to reporters? This is a great way of cutting through company politics, short-termism, vested interests and local expediency to get to the “right thing” to do. Remember the right decision is often the hardest.

2. Refine and improve your risk-based decision making skills. Always be structured and consistent in your approach and remember decision making is a skill that can be learned, refined and improved.

3. As you move up the ladder always remain visible, connected and available. You need to keep your finger on the pulse.

4. Change your attitude to problems and mistakes. When something goes wrong, focus on the learning gained. Concentrate on the problem, not the person. You will be amazed how much progress you will make.

5. Remember there is risk in everything. Perfect your risk assessment skills but remain balanced and pragmatic. The more risk averse you become, the greater the risk.

6. It’s vital you never lose the trust and respect of your colleagues and the regulator. Maintain your honesty, integrity and transparency no matter what.

7. When faced with any challenge, always remain part of the solution, not the problem, and never use fear to get what you want. You only get away with it once.

8. Never surround yourself with people who only agree with you. You want colleagues to challenge and question your decisions. Resolve disagreements by exploring differences of opinion, not defending them.

9. You are not the font of all knowledge. If you want respect, just admit you don’t have the answer. Humility goes a very long way in gaining respect.

10. When you have to make tough decisions, take time to explain why to those impacted – your rationale, your reasons. Above all, always be consistent and pragmatic. Don’t make mountains out of molehills.

11. Leadership can be lonely. Work hard to create and maintain strong relationships in all areas of the business and make sure that you continue to learn from each one of them and provide them support in return. You get back what you put in. The best leaders are those with the strongest networks.

12. Remember it’s your relationships that dictate how successful you are. Treat people in the way you wish to be treated.

13. Be expected to have opinions on everything. Opinions are good. They are based on principles that run deep as a result of your training and experience. Remember that facts are your friends. As facts change, change your opinion but never change your principles.

14. Listen twice as much as you talk. Remember, listeners control conversations.

15. Get yourself some good mentors. People who listen and advise but give you the freedom to decide.

16. If it’s popularity you’re after, you are in the wrong job. Just make sure you are respected, not feared.

17. Never be pushed into decisions on the spot; take time to reflect. Decisions made when stressed and tired are usually wrong.

18. When communicating with senior management, use their language not the language of QA. Always provide options that make business sense. Explain your reasons and rationale. Lastly, communication is measured by the response you get. If it’s not what you expected, change the way you communicate.

19. Provide good education and training to cross-functional teams. You can then delegate with confidence.

20. There will be times of extreme pressure and stress, so be prepared. You will need to develop skills and mechanisms to do this at home and at work. Remember your health and relationships at home matter most. Take either for granted and you will be in trouble.

21. Always lead by example, and maintain transparency and consistency in all that you do. Remember everyone views the world differently and no-one thinks like you.

22. Plan your professional development for the future. You are never too old or wise to learn something new.

23. Always keep up to date and fresh; don’t let technology pass you by. Every day is a learning opportunity.

24. DBA may have morphed into NSF, but it’s the same people. They have been there and done it and have acted on more than one occasion. Keep them on your speed dial list. From my experience, they genuinely care.

25. Always challenge the status quo; never accept it. It’s only those who push the boundaries that make progress.

26. Become an 80/20 person in your thoughts and actions. Focus on the 20 percent that really matters… You can’t do everything. Remember energy follows thought so only focus on what matters. Do the basics better than anyone else.

27. Sometimes the situations you face may appear overwhelming. Just tackle whatever you’re faced with one bit at a time.

28. If you make the development of your people your priority, you will never be short of followers.

29. Invest in quality thinking time away from distraction one hour each day.

30. Never allow people in your charge to forget the importance of what they do in making medicines that matter. If you are not passionate about what really matters, why should they be?

Next Steps:

• Print this off
• Discuss with colleagues
• Review it daily (put it above your desk)
• Commit to learning from the very best – those that have been in your shoes and understand your world
• Remember to give us a call at any time – we are only at the end of the phone if you need some free advice. We will guarantee you absolute discretion, honesty, support and solutions.

One last word. You don’t have to do any of this at all. Survival isn’t compulsory.
**Forthcoming Courses**

**What’s planned for January – March 2015**

### EU Courses:

**Formulation & Processing, Part 1**
Ever wondered how drugs get into the body and get to the target sites? Ever considered why solid dose manufacture is often so hard to control and understand? Practice and understand some of the tough QA and QP decisions found with these products.

**January 19-23**
Hilton York Hotel, York, UK

**GMP for Biological and Biotechnology Products**
How does bioproduction differ from small molecule synthesis, where are the key risks and how are they mitigated? Make sure that you are ‘in the know’ and can influence change effectively at your facility.

**February 3-5**
Manchester Marriott Victoria & Albert Hotel, Manchester, UK

**How to Audit – Bulk Biotech Operations**
Auditing bulk biotech operations requires a modified approach and skill-set, find out why and help ensure cGMP is maintained at your facility.

**February 6**
Manchester Marriott Victoria & Albert Hotel, Manchester, UK

**Pharmaceutical Packaging**
Increasing supply chain pressures and legislation, from starting components to patients, mean that pharmaceutical packing, and the GMP of packing and the supply chain are increasingly a focal point for all in the industry.

**February 10-12**
Carlton President, Utrecht, The Netherlands

**Risk-Based Decision Making for Qualify Professionals and QPs**
Detecting, assessing and mitigating risks to product quality and GMP compliance is a crucial step in building a sustainable business. Find out how to do it quickly, accurately and with proven return on investment.

**March 3-4**
Amsterdam Marriott Hotel, Amsterdam, The Netherlands

**Pharmaceutical Legislation Update**
Keep up-to-date with the latest regulatory requirements.

**March 25**
Renaissance Manchester City Centre Hotel, Manchester, UK

### US Courses:

**Human Reliability Improvement Program**

In-House – We Come to You!

**Objective:** Reduce error re-occurrence and repeat deviations attributed to Human Error by 50% within one year

**How:** By understanding the science of human error, following a structured approach to investigations, and applying NSF’s tools for Human Factor analysis to identify the most effective CAPAs

**Outcome:** Significant cost savings in time and expense!

**Next steps:** Attend our March 27th webinar on Documentation Error Reduction and learn more about the NSF Human Reliability Program. For additional information on this program or our other US offerings, contact Jim Morris at jmorris@nsf.org

**Book your place at:** www.nsf.org/info/pharma-training
FREE ‘MASTER CLASS’ WEBINARS
PRESENTED BY MARTIN LUSH, PRESIDENT, NSF HEALTH SCIENCES PHARMA BIOTECH

We are passionate about helping our clients prepare for the future, not the past. We have been in your shoes so we really understand the challenges you face. These free webinars will provide the skills and knowledge to help keep your life as simple as possible. The 150 free places are available on a first come first served basis. Just go to our website for exact dates, times and the registration process. Book early, the last one was fully booked within 30 minutes!

January:
How to improve human reliability

February:
Improving CAPA effectiveness to drive down repeat incidents

March:
How to establish the right quality habits in the workplace

April:
The practice of risk-based decision making

May:
Changing behaviors in the workplace – how to educate, not train

June:
The art and science of simplification – how to win your war on complexity

October:
Change control – best industry practices

November:
Risk management – best industry practices

December:
Contamination control – how to protect the purity of your products