The Journal of NSF-DBA Issue 17 Winter 2011

NSF DBA℠

25 YEARS OF EXCELLENCE

Years of Service to the Pharmaceutical Industry

An NSF International Company

www.nsf-dba.com

welcome

Bob Pietrowski
Managing Partner
NSF-DBA

Welcome to this very special edition of the DBA Journal. This year marks the 25th anniversary of our company – a quarter of a century of support to the pharmaceutical and healthcare industries worldwide. We started with just two people in April 1986 and we have grown to be a premier consultancy with over 50 consultants and support staff on three continents. There are many thousands of reasons for our success – you our clients. We would like to thank all of you for your support over the last 25 years; you have made our work a real pleasure and we hope we have repaid your faith in us.

In this special edition of the Journal we take a backward look at the development of NSF-DBA and chart some of the key moments for us. Some of you may remember sharing those times with us. We also look forward to the future and we hope that you will be an important part of that too.

As we are in retrospective mood, we also review some of the Tech Talk articles from previous issues of the Journal and ask "Has anything changed since this was published?" We hope you find this thought provoking.

The next 25 years will be no less of a challenge than the last 25, for the healthcare industry as well as for NSF-DBA, and we look forward to meeting that challenge with you.

Bob Pietrowski
Managing Partner

NSF DBA℠
25 YEARS OF EXCELLENCE

International Healthcare Consulting & Education Experts

NSF-DBA's Eleventh Qualified Person Series just starting as we celebrate our 200th Qualified Person in the Industry

NSF-DBA's tenth series of QP training proved to be successful in continuing to generate new QPs into the industry. Here at NSF-DBA we never get blasé about their success, quite the opposite; we continue to be delighted by the notifications from our delegates that they have passed their QP viva or have been accepted to work as a QP in the UK or other member states.

We recognise that this represents the culmination of two or more years of hard work and dedication by the individual. This also impacts on partners and families, without whom these trainees could not achieve this level of success.

In fact we are so proud of our delegates' successes that we thought we should mark a significant milestone for NSF-DBA, like the 200th trainee gaining QP status. It is a pleasure therefore to announce that this accolade goes to Shawn Murtough from Penn Pharmaceuticals. Shawn will be enjoying a weekend in London and a 'Red Letter Experience Day' as our guest (and we can assure you Mike Halliday will not be present!). Shawn has promised to send us some photographs from these events and we will share these with you in the next edition of the Journal.

For those of you counting down for the next milestone, we are currently standing at 210 QPs and the list is growing on a regular basis!

We would also like to congratulate other recent additions to the UK QP register:

Giby George
Reckitt Benckiser Healthcare (UK) Ltd

David Jamieson
AstraZeneca Pharmaceuticals

Peter Kendrick
Cephalon (UK) Ltd

Chris Forrest
AstraZeneca Pharmaceuticals

John Horry
Reckitt Benckiser Healthcare International Ltd

James Culyer
Napp Pharmaceuticals Ltd

Jonathan Dormer
UCB Celltech Ltd

and one of our European trainees:

Stefan Verstegen
Intervet Schering-Plough Animal Health, The Netherlands

Tech Talk

A Review of some past Tech Talk Articles

with Martin Lush and Bob Pietrowski

Human Error: Causes and Prevention

Original Article:

Back in 2008 many companies were struggling with 'human error', that convenient excuse for anything that goes wrong. From deviations, customer complaints, product recalls through to warning letters! DBA's opinion is quite simple. *Nobody goes to work to do a bad job and make mistakes. Human error is not the cause of the failure, but the effect. Human error can never ever be the conclusion of any investigation, only the starting point!* The article then summarised some simple tools and techniques to reduce human error. Two years on the question is "did they work?" Well the answer is a resounding "yes", providing they are implemented correctly!

Where Are We Now?

We've presented our 'error prevention' course to many companies. Techniques are described in detail and practiced and refined by all. But do they work in 'real life'? Well, here's some client feedback:

'The complexities of our Batch Record led to many mistakes and errors. We used DBA's 'simplification techniques' to reduce our BR size by 60% in just 12 months. The simplified version is almost error free and a lot more efficient'

'Lean Team Leader'. CMO Company. UK

'Errors are often introduced by poor decision making. We now use the decision making and problem solving process covered on DBA's course. Decision making is now more fact based and standardised.

'Technical Team Leader'. Biotech Company. US

Before designing our 'Human Error: Causes and Prevention' programme we consulted widely with colleagues in the nuclear, automobile and aerospace industries, leaders in the field of error reduction. What we learnt formed the basis of the tools and techniques we've designed. Two years on we've proved that if you apply the same leadership and methods you get the same result; an almost error free workplace. So, if your objective is to improve compliance and reduce costs by error proofing your processes and procedures please give me a call on 01751 432 999 or email me at mkl@nsf-dba.com

Goodbye to Fear, Doubt & Anxiety – Hello to Extreme Uncertainty?

In Issue 9 (Summer 2008) we argued that recent changes to European Union GMP requirements meant that FDA cGMP regulations were no longer the strictest in the world – it is now EU inspectors, not FDA investigators, who are feared internationally. To back up this view, we quoted EU requirements for…

- Clinical Trial Manufacture
- Sterile Products Manufacture
- Quality Management Systems
- Risk Management
- Raw Material Control
- Computerised Systems
- Biopharmaceuticals Manufacture
- Batch Release and the Role of the QP

So has anything changed?

Clinical Trials Manufacture

Since Summer 2008, FDA has forced through changes to remove Phase 1 clinical trials from compliance with the full range of cGMP regulations. There has been no such relaxation in the EU.

Sterile Products Manufacture

There has been no change to the fundamental requirements in Annex 1. EU GMP still requires monitoring of 5 micron particles and the requirements for protection of capping operations and application of the zoning principle for controlled environments remain more stringent than US expectations.

Quality Management

There has been no change in either EU or FDA expectations. EU requirements remain more stringent than those of FDA despite the adoption of ICH Q10 in both areas.

Risk Management

EU regulators continue to embrace risk management with almost religious zeal – so much so that risk management is in danger of becoming an industry in its own right, as validation did twenty years earlier. FDA has also embraced the principles in ICH Q9 but, we believe, in a less dogmatic and more pragmatic way.

Raw Material Control

While events surrounding heparin and other materials have hardened FDA's approach to the control of raw materials, EU requirements for sampling and testing of incoming lots of raw material still far exceed FDA requirements.

Computerised Systems

It remains to be seen whether the final version of Annex 11, expected imminently, will bring EU expectations closer to the more pragmatic requirements of FDA.

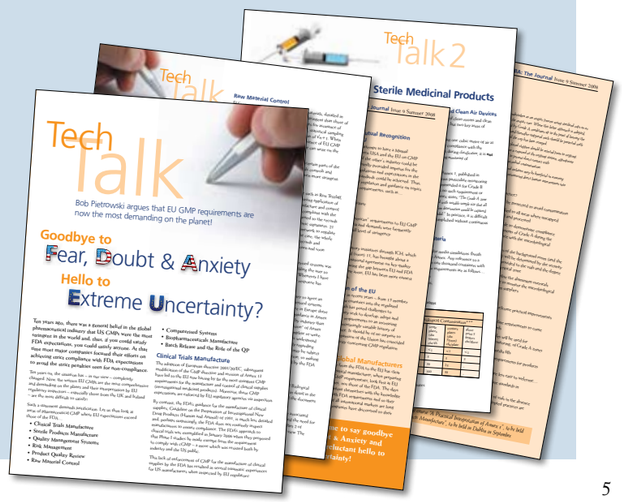
Biopharmaceuticals Manufacture

The latest draft of Annex 2 has, thankfully, addressed many of the concerns expressed by industry following the release of the first draft revision. There is now reason to believe that the final document will represent a balanced and valuable addition to GMP guidance. It is regrettable that FDA has yet to update their ageing inspection guideline of 1991.

Batch Release and the Role of the QP

EU procedures for batch release remain the most onerous in the world. Sadly, there has been no diminution in the demands placed upon the poor QP by European regulators; on the contrary, these demands have increased.

Overall, therefore, little has changed. EU GMP regulations and expectations remain the most demanding on the planet. Does this mean, therefore, that patients in the EU are better protected than their counterparts in the rest of the world? We will leave you to answer that question.



Bob Pietrowski, Managing Partner, reflects on the journey for David Begg Associates

1980s The Birth of a Vision

In the early 1980s, David Begg was a senior GMP inspector with the UK pharmaceutical regulatory agency. He had joined the agency in the wake of the first UK medicines legislation because he was a passionate believer in Good Manufacturing Practice and its critical contribution to product quality and patient safety. He wanted to help the pharmaceutical industry improve to help society. However, by 1985, David was convinced that he could make an even greater contribution to the industry he loved by leaving the regulatory agency and providing consultancy directly to pharmaceutical companies. This was a logical extension of his work as a GMP inspector, but he strongly believed that the greatest contribution to product quality could be made, not just by traditional auditing and consulting, but rather by working with those people who really influence the safety and quality of medicines – the people who make them, test them and maintain the equipment, utilities and premises. In particular, David believed passionately in training and development of people as the most effective means of Quality Assurance. As David

David Begg in the early days

used to say "People are the most important active ingredient in any process!"

David explained his vision of a new kind of consultancy – one which placed emphasis on developing people at all levels – to trusted colleagues in the industry and was given assurances that if he were to create such a consultancy, they would be enthusiastic customers. So David convinced his colleague, Ian Sykes, to leave the agency with him and in April 1986 David Begg Associates was born. The first 'offices' were above David's garage at his home near York and it must be said that the initial year or so was a challenge. There were many days when the telephone never rang! But, slowly and steadily, the business grew as companies discovered the quality of David's work and its impact on their staff.

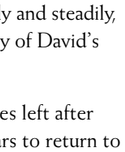
All work and no play makes David very tired (l to r Peter Smith, Mike Bowsher and David Begg)

Ian Sykes left after two years to return to industry, but David was joined by Mike Bowsher, an old friend and future owner of the company, and by Peter Smith, who had worked with David for the UK regulatory agency. After a difficult start, David Begg Associates had grown to be an established and highly respected consultancy. The vision had been realised.

1990s A Period of Expansion

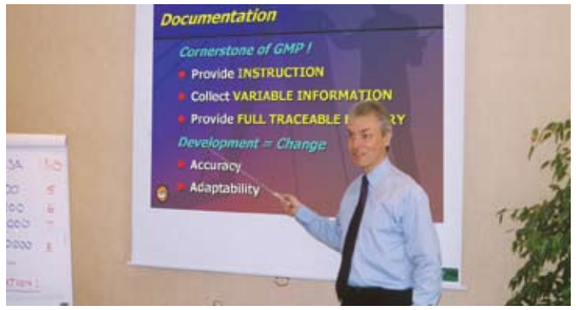
The 1990s saw David Begg Associates build upon its beginnings to become firmly established as one of the premier pharmaceutical consulting and training organisations in Europe. It soon became clear that more consultants were required to satisfy demand – and that meant moving to proper offices. So it was in late 1989 that David Begg Associates moved from David's home to Kirkbymoorside, just a few kilometres away. Three young Partners were recruited from the UK pharmaceutical industry (Bob Pietrowski, Sue Mann and Martin Lush) and several independent Associate Consultants joined the growing group. This major increase in staff and associated specialisms enabled David Begg Associates to grow at an unrivalled pace.

Gerry Migliaccio,
Vice President, Global Quality Operations,
Pfizer Inc. USA



The results surpassed our expectations. The QA leaders who participated in the training now have much greater confidence in their decision making ability. DBA provided training that could be immediately used in their daily activities.

At the same time, David Begg Associates followed David's vision by developing innovative training courses for the pharmaceutical



Bob Pietrowski presenting training – always a key element for DBA

industry. Of all these initiatives, none was more important and successful than Qualified Person training. Again, it was David who saw the need for a structured, industry-based training programme for quality professionals wishing to become QPs. Training did already exist, notably at the University of Sunderland in the UK, but David Begg Associates firmly believed that QP training should combine academic education with pragmatic teaching from industry veterans. A partnership was formed with the University of Strathclyde in Scotland and our first QP training began in late 1990. From those early days, QP training from David Begg Associates and the University of Strathclyde has grown in stature to be a widely acknowledged industry leader and hundreds of quality professionals from all over Europe have gained QP status after following our courses.

QP training, along with an unsurpassed reputation for the growing portfolio of other training courses as well as for the quality and pragmatism of auditing and consulting, helped David Begg Associates grow to be perhaps the most successful consultancy in Europe by the end of the twentieth century.

Johan Hanselaer,
Vice-President, Quality, Industrial Operations
Sanofi-Pasteur, France

The Quality Enhancement Program is one of the fundamental success factors for the integration of new business entities into Sanofi-Pasteur. The highly interactive program offers detailed and practical understanding of the legal, regulatory and technical elements of our business, thereby enhancing the knowledge, experience, confidence and decision making skills of our colleagues.

2000s The Globalisation of David Begg Associates

The strong foundation laid in the 1990s enabled David Begg Associates to truly internationalise its activities in the new millennium. From its traditional base in the UK, David Begg Associates added training locations in Ireland, The Netherlands, Singapore and Puerto Rico. The educational courses in Puerto Rico were particularly important in introducing David Begg Associates to the US pharmaceutical industry. Already well known and respected as a consultancy which could assist US companies to achieve success in European regulatory inspections, more and more clients now recognised David Begg Associates as a provider of high quality education and staff development. Soon, David Begg Associates was helping forward thinking US companies to develop their key staff through modular, in-house education programmes similar to the QP training offered in Europe. David Begg finally retired and new Partners, Mike Halliday and Pete Gough, joined David Begg Associates to assist in this new growth.

A young looking Martin Lush

Then in 2007, David Begg Associates was acquired by the US company, NSF International, and became DBA. Mike Bowsher retired at this time. The new owners committed to help DBA grow into a truly global consultancy and with NSF's constant support, growth has been rapid and spectacular. A US office was opened in Boston in 2008 and, since then, Partners Jim Morris and Neil Wilkinson, along with their constantly growing team of Associate Consultants, have grown the company in leaps and bounds. Critical to this growth has been the introduction of a modular education programme, the Quality Leadership Program, which is based on the European QP training. Successful students have the opportunity to gain a Masters Degree from the University of Strathclyde. The popularity of this programme has exceeded all expectations. This and other initiatives helped the US company to grow by over 50% in 2010. In addition, our dietary supplements consultancy in the US, led by Casey Coy, is growing day by day and in 2011 will offer modular education, similar to the Quality Leadership Program, for dietary supplements quality professionals.

But international growth has not been limited to the USA. DBA now has an office in South Africa, headed by Allan Thomas, and DBA is constantly looking to offer its services through local representation in Europe and internationally. Additionally, DBA constantly seeks to broaden its scope of consultancy, for example into medical devices.

None of this would have been possible without the support and encouragement of NSF International. It is for this reason that we are proud to mark our 25th anniversary by formally changing our name to NSF-DBA.

The Future

What will the next 25 years hold for NSF-DBA? We cannot be certain, but we are committed to ensuring that wherever and however the pharmaceutical, medical device and dietary supplements industries establish themselves globally, NSF-DBA will be there to provide support to companies and their people.

The original vision of David Begg Associates lives on.

Getting More from your Training Budget

With training budgets getting the squeeze, more and more companies are scrutinising the effectiveness of their training programmes, asking "are we getting value for money?" As the numbers of warning letters and consent decrees reach unprecedented levels regulators are also questioning the effectiveness of training programmes.

So how effective is yours? Well, if a recent survey is anything to go by, the answer doesn't make pleasant reading. McKinseys conducted a survey of over 1400 companies, including many in the pharma sector ('Building Organisational Capabilities. McKinsey Global Survey Results March 2010'). Their conclusions:

- **The 'vast majority of training programs are ineffective and failed to improve understanding and performance'**
- **That training methods have remained very traditional and that many companies have failed to adopt a more effective and scientific approach**

Clearly a lot of time and resource are being wasted and valuable training budget squandered.

Thanks to vast amounts of research into 'adult learning' we now know how to improve training effectiveness. In fact, NSF-DBA has been applying these principles for years in course design and delivery. This is probably why delegates keep telling us our courses are 'unique', 'memorable' and 'different'.

So, improving the effectiveness of your training programme and getting more from your training budget is possible, providing you get the basics right! Here some essential rules to follow:

1. Get people in the mood!

All learning is what we call **'state dependent'**. If people don't want to learn, if they are not 'in the mood', you're wasting your time. I had the pleasure of experiencing a GMP 'refresher' training session recently. Operators, most of which didn't want to be there, dutifully filed in at the end of their long shift. Most were tired, hungry and thinking of their commute home. A few acknowledged the heroic antics of the trainer and the seemingly endless stream of PowerPoints. I lost count at 35. A short questionnaire followed, before the 'GMP refresher training' box was ticked. Job done, at least for another year. Did everyone pass the 'assessment'? Of course. Will the training add value and improve performance? I doubt it. Will the company get a 'return on its investment'? Not in a million years.

Remember:

- People only learn if they want to; you can't force people to learn anything. The job of your training provider is to ensure people are open to learning, keen, willing and able. This takes real skill
- Stress and fatigue kill effective learning every time. The training environment must be informal and welcoming. Everyone must feel safe and relaxed… do everything possible to avoid the 'classroom' layout and 'feel'
- Make it participative. Learning is an active, *not* a passive process
- Inject plenty of variety
- Above all, make it fun. If you haven't got a laugh in the first few minutes it's going to be a long and fruitless session

If you want to change behaviour and improve performance get everyone in the mood first!

2. Satisfy everyone's 'Preferred Learning Style'

- Although our brains have infinite capacity we all absorb information differently
- Some of us are **visual learners**, preferring pictures, diagrams, mind maps and the like. In fact, anything other than words
- **Auditory learners** on the other hand, learn best from the discussions
- **Kinaesthetic learners** 'learn by doing'. They have to get their hands dirty. For these folks classroom sessions are boring and tedious and completely ineffectual
- The fourth group are the **Intellectual** learners who learn through problem solving

So, if you want your training to be effective find out the learning styles of your audience and then design your programme accordingly. The days of 'death by PowerPoint' are long gone. Every NSF-DBA course is designed to meet all learning styles, not just one or two.

3. Switch on their 'Reticular Activating System'. The 'doorway' to effective learning

- Our brain has an awful lot to cope with. On top of keeping our vital organs and systems running smoothly, no mean task, it must also make sense of the external world. In fact it's bombarded by *billions* of information 'bits' every minute of every day. To prevent cerebral meltdown, evolution has provided us with a neat little filtering system called the RAS (The Reticular Activating System). This is the part of our brain that decides what enters our long term memory and what stays out. If you don't activate the RAS, the door remains closed and information is soon forgotten.

RAS activation is vital. Without this nothing is absorbed and trainers, even the best performers, are wasting their time. Our tutors know how to 'flick the switch' within minutes.

4. All learning is 'subconscious'

Information is first absorbed by our conscious 'working brain'. The only problem is this has very limited capacity and no long term memory capability; in fact it can only cope with 7 facts +/- 2 at any one time! This is the part of our brain that remembers telephone numbers and the like, but not for long. For effective learning to take place information must be moved from the working, conscious brain, to subconscious brain quickly, ideally within 30-40 minutes.

If you don't move the information from the working brain quickly it will be lost for ever.

5. Turning 'information' into improved performance: Replacing old habits with new ones

NSF-DBA courses are designed to change the way people think and act. This is easier said than done because we are all creatures of habit. Over time any repetitive task, even ways of thinking, become a habit. People act without consciously thinking about what they are doing. When 'training' introduces something new our brains really struggle, preferring to stick with the old ways of thinking. In fact, old habits are actually impossible to break. They can only be replaced with new ones which, through repetition and practice, become stronger. Although 'old habits die hard' those of you who have attended our courses will be familiar with the techniques we use to accept new ways of thinking.

Skilled trainers have the tools and techniques to replace old habits with new ones.

To assess the effectiveness of your training provider ask four simple questions:

- **"How do they get people 'in the mood'?" …if they don't know they're wasting your money**
- **"How do they identify participants' learning styles and design sessions to accommodate all four?"**
- **"How do they flick the RAS switch?" …or do they leave the door closed?**
- **"How do they weaken old habits and replace them with new ones?" …if they don't old behaviours and ways of working will remain**

At NSF-DBA we practice what we preach; our objective is to educate, not train. There is a big difference.

'Education is what survives when what has been learned has been forgotten'

We design our in house and residential courses to change the way people think and therefore behave. They leave us able to make a difference.

By adopting these methods our customised 'in house' courses are renowned for acting as a catalyst for lasting change and improvement.

Before every course we:

- Work with you, our clients, to really understand
  - The motivation behind the course (the big picture)
  - The background and experience of the target audience
  - Your company's products, processes and procedures
  - Any specific 'learning objectives'
- Design the course to suit all learning types
  - Customised team work exercises for the kinaesthetic learners
  - High quality presentations for the visual types
  - Very comprehensive course books (not just slides) to satisfy intellectual learners as well as provide an invaluable reference for years to come
- Help you provide a training environment that is an ideal learning environment
- Provide you with the best tutors that money can buy. With an average of 28 years 'hands on' experience our tutors have that rare ability to inspire, engage, entertain and educate… not just 'pass on' information

Although we're constantly striving to get better our clients tell us we do a pretty good job. Just visit our website and have a look at the course feedback comments. The phrase *'I learnt a lot'* crops up regularly.

As many of you know, our QP education programme has been running for almost 20 years. Over this period **96% of NSF-DBA candidates pass** the rigorous, independent assessment process. How we educate seems to work; what we teach seems to 'stick'.

David Begg used to say

'If you think training is expensive, try ignorance'

For the short-sighted, training is usually seen as a cost, not an investment. For others it's the life blood of their company. Ongoing education is a must if you want the motivated, flexible and multi-skilled workforce so vital to your future. Whichever camp you fall into one thing is for sure… training effectiveness must be improved.

If you need help in getting more from your training budget or more information on the tools and techniques for effective training contact me at mkl@nsf-dba.com

Forthcoming Courses

What's planned for January – March 2011

NSF DBA SM
25 YEARS OF EXCELLENCE
International Healthcare Consulting & Education Experts

Formulation & Processing (Part 1)

Qualified Person & Professional Development Training

Hilton York Hotel, York, UK

17 – 21 January 2011

First of a two part module designed to provide pharmaceutical quality professionals with essential knowledge of formulation requirements and key processing methods (and critical control points) for the major pharmaceutical dosage forms.

Course Fee: **£3200.00 plus VAT** (First Booking)
£2560.00 plus VAT (Additional Bookings from same site)

Pharmaceutical GMP

Glenhove Conference Facility, Johannesburg, SA

26 – 28 January 2011

Europe's most popular GMP course! An excellent overview of WHO EU and US GMP regulations, plus up to the minute guidance on the latest 'hot topics'.

Course Fee: **R6760.00** (First Booking)
R5408.00 (Additional Bookings from same site)

Pharmaceutical Packaging (QLP8)

Quality Leadership Program

Royal Sonesta Hotel, Boston, MA, USA

1 – 3 February 2011

This course is designed to teach the aspiring Quality Leaders or technical professional all they need to know about packaging materials, regulations regarding labelling, the essential GMPs of packing operations and new initiatives regarding counterfeiting, etc. Includes a visit to a supplier of pharmaceutical packaging and labels.

Course Fee: **$2700.00** (First Booking)
$2160.00 (Additional Bookings from same site)

Workshop on HVAC for Biopharmaceutical Facilities and Clean Utilities for Biopharmaceutical Facilities

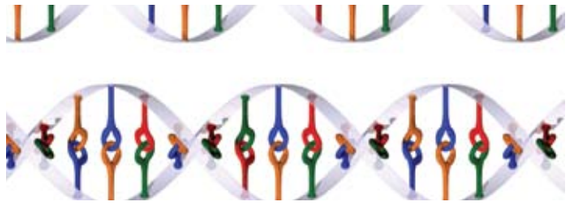
Royal Sonesta Hotel, Boston, MA, USA

4 February 2011

HVAC for Biopharmaceutical Facilities – Morning 08:30-12:00
This training will provide an overview of HVAC systems for biopharmaceutical operations. We will examine the role of HVAC in maintaining appropriate room classification and practical considerations. We will also touch on commissioning and qualification approaches.

Clean Utilities for Biopharmaceutical Facilities – Afternoon 13:00-16:30
We will review clean utilities including water, clean steam and gases used in biopharmaceutical manufacturing. Key design and operating requirements will be reviewed, from a regulatory point of view, comparing US and EU requirements, along with practical considerations. We will discuss points to consider for commissioning and qualification of each system.

Course Fee: **Half Day $300.00** **Full Day $500.00**



GMP for Biological and Biotechnology Products

Manchester Marriott Victoria & Albert Hotel, Manchester, UK

15 – 17 February 2011

This course is designed for those with relatively little experience of applying GMP requirements to the manufacture of biologicals and biotech products. We will describe all the stages of biopharmaceuticals manufacture, from cell bank to finished product, and explain the key GMP and quality-critical issues for each and how to comply. If you are new to the biotech industry or a QP who has to take responsibility for this group of products, this course is for you.

Course Fee: **£1740.00 plus VAT** (First Booking)
£1392.00 plus VAT (Additional Bookings from same site)

Practical Application of Quality Risk Management

Glenhove Conference Facility, Johannesburg, SA

23 – 25 February 2011

The latest 'hot topic' in GMP! Both the EU and FDA have stated they will use risk assessment in their inspections and expect manufacturers to adopt risk-based quality systems based on guidance provided in ICH Q9 (Pharmaceutical Risk Management). Come and learn what exactly is expected and how to apply risk management techniques to your quality operations.

Course Fee: **R6760.00** (First Booking)
R5408.00 (Additional Bookings from same site)

Preparing for the Future: Successful Implementation of ICH Q8, 9 and 10

Manchester Marriott Victoria & Albert Hotel, Manchester, UK

1 – 3 March 2011

The development of ICH Q8 (Pharmaceutical Development), Q9 (Quality Risk Management) and Q10 (Pharmaceutical Quality System) has set the route map for pharmaceutical quality management into the future. This course will explain why these guidelines are so important and provide you with practical advice on how best to implement them to achieve maximum benefit. Expert speakers from industry and regulators will present their views and experiences of implementation.

Course Fee: **£1740.00 plus VAT** (First Booking)
£1392.00 plus VAT (Additional Bookings from same site)

Achieve Operational Excellence: Deviation and CAPA Systems – How to Simplify and Improve

Manchester Marriott Victoria & Albert Hotel, Manchester, UK

7 – 8 March 2011

This focused, two day course will provide you with proven tools and techniques to simplify your deviation management system and improve the effectiveness of your CAPA system, saving you time and money whilst improving regulatory compliance.

Course Fee: **£1320.00 plus VAT** (First Booking)
£1056.00 plus VAT (Additional Bookings from same site)

Formulation & Processing (Part 2)

Qualified Person & Professional Development Training

Hilton York Hotel, York, UK

7 – 11 March 2011

Second of a two part module designed to provide pharmaceutical quality professionals with essential knowledge of formulation requirements and key processing methods (and critical control points) for the major pharmaceutical dosage forms.

Course Fee: **£3200.00 plus VAT** (First Booking)
£2560.00 plus VAT (Additional Bookings from same site)

Successful EU GMP Inspection Management

Bethesda Marriott Hotel, Bethesda, MD, USA

8 – 10 March 2011

This course is designed to help you to avoid the difficulties experienced by some of your colleagues by preparing you for a European inspection.

Course Fee: **$2675.00** (First Booking)
$2140.00 (Additional Bookings from same site)

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

Manchester Airport Marriott Hotel, Manchester, UK

9 March 2011

The Qualified Person and other Technical Personnel need to be informed and aware of pharmaceutical legislation. Changes in legislation and guidelines, and the interpretation of them, can have significant implications for the individual and their company. This is a one day seminar that is designed to form part of your Continuing Professional Development.

Course Fee: **£695.00 plus VAT** (First Booking)
£556.00 plus VAT (Additional Bookings from same site)

Achieve Operational Excellence: Change Management Systems – How to Simplify and Improve

Manchester Marriott Victoria & Albert Hotel, Manchester, UK

9 – 10 March 2011

The control of changes is perhaps the greatest challenge facing us in today's climate. We will provide you with proven techniques to simplify your change control systems, making them quick and efficient whilst at the same time ensuring compliance with all regulatory requirements.

Course Fee: **£1320.00 plus VAT** (First Booking)
£1056.00 plus VAT (Additional Bookings from same site)

Meeting the Regulatory Requirements for Clinical Trials in the EU

Royal Sonesta Hotel, Boston, MA, USA

15 – 16 March 2011

This course will give you all you need to comply with EU expectations. If you currently supply clinical trial materials to Europe, or if you plan to in the future, it is essential that you fully understand the European regulatory framework for clinical trials, the rigorous GMP requirements for the manufacture and packing of clinical supplies, the unique role of the Qualified Person and what EU regulators will look for during inspections.

Course Fee: **$1775.00** (First Booking)
$1420.00 (Additional Bookings from same site)

Human Error: Causes and Prevention

Manchester Marriott Victoria & Albert Hotel, Manchester, UK

15 – 17 March 2011

Human error is a commonly quoted cause of problems and deviations in our industry, but it is often not the real reason. just a convenient excuse, and so corrective actions such as 'retraining' are doomed to failure. You know that and so do the regulators! This unique course will help you to see beyond 'human error' as the root cause of problems. We will show you why people make mistakes and provide you with practical ways to reduce errors in the workplace.

Course Fee: **£1740.00 plus VAT** (First Booking)
£1392.00 plus VAT (Additional Bookings from same site)

And remember that from 2011 companies based in Europe (not including UK) will be exempt from VAT charges when you provide us with your VAT number.

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Forthcoming Courses

What's planned for March – April 2011

NSF DBA SM
25 YEARS OF EXCELLENCE
International Healthcare Consulting & Education Experts

Devising a Regulatory Submission Strategy for the EU

Royal Sonesta Hotel, Boston, MA, USA

17 March 2011

This course will give you an introduction to the types of issues that need to be considered in order to prepare a regulatory strategy and smooth the passage of your product to the EU market. Devising a clear, well thought out strategy early in development is critical for success. By attending this course you will become familiar with the key strategic considerations necessary to meet the regulatory agency (EMA and/or national) requirements and understand why early consideration of these issues is crucial to success.

Course Fee: **$950.00** (First Booking)
$760.00 (Additional Bookings from same site)

Practical Aspects of Pharmaceutical Validation

Manchester Marriott Victoria & Albert Hotel, Manchester, UK

21 – 24 March 2011

This ever-popular course will provide you with sound, practical advice on how to organise, document and manage all aspects of qualification and validation to meet international GMP requirements. In particular, we will review and discuss FDA's latest proposals for validation, which could spell the end of the 'magic' 3 batches!

Course Fee: **£2275.00 plus VAT** (First Booking)
£1820.00 plus VAT (Additional Bookings from same site)

Process Validation – The New Paradigm

Manchester Marriott Victoria & Albert Hotel, Manchester, UK

24 March 2011

The publication of ICH Q8, 9 and 10, and the work to produce ICH Q11, has lead to a paradigm shift in the way pharmaceutical products are developed and subsequently validated. The new approach to development is now referred to as Quality by Design (QbD) and this has resulted in both the US FDA and the EU CHMP radically re-thinking the concept of process validation.

You can join just day four of NSF-DBA's course on Validation. This will help you benchmark your current approach to process validation against the new regulatory expectations.

Course Fee: **£695.00 plus VAT** (First Booking)
£556.00 plus VAT (Additional Bookings from same site)

Preparing for the Future: Successful Implementation of ICH Q8, 9 and 10

Glenhove Conference Facility, Johannesburg, SA

23 – 25 March 2011

The development of ICH Q8 (Pharmaceutical Development), Q9 (Quality Risk Management) and Q10 (Pharmaceutical Quality System) has set the route map for pharmaceutical quality management into the future. This course will explain why these guidelines are so important and provide you with practical advice on how best to implement them to achieve maximum benefit. Expert speakers from industry and regulators will present their views and experiences of implementation.

Course Fee: **R6760.00** (First Booking)
R5408.00 (Additional Bookings from same site)

Sterile Products Manufacture

Manchester Marriott Victoria & Albert Hotel, Manchester, UK

28 – 31 March 2011

One of our most popular courses. A comprehensive, four day course on the latest EU and US GMP requirements for sterile products manufacture, plus practical advice on how to ensure compliance in a cost-effective and scientifically sound way.

Course Fee: **£2275.00 plus VAT** (First Booking)
£1820.00 plus VAT (Additional Bookings from same site)

Human Error: Causes and Prevention

Bethesda Marriott Hotel, Bethesda, MD, USA

29 – 31 March 2011

Human error is a commonly quoted cause of problems and deviations in our industry, but it is often not the real reason, just a convenient excuse, and so corrective actions such as 'retraining' are doomed to failure. You know that and so do the regulators! This unique course will help you to see beyond 'human error' as the root cause of problems. We will show you why people make mistakes and provide you with practical ways to reduce errors in the workplace.

Course Fee: **$2675.00** (First Booking)
$2140.00 (Additional Bookings from same site)

Quality Management Systems (QLP9)

Quality Leadership Program

Royal Sonesta Hotel, Boston, MA, USA

4 – 6 April 2011

We all know that the quality of your products depends on the quality of your people and the effectiveness of your Quality System. In fact, as Qualified Persons and Quality Professionals, you can't release product and stay in business unless your QMS is 'in control'. This is easier said than done. Supply chains are more complex than ever before and you are being asked to do more with less, and faster!

Course Fee: **$2700.00** (First Booking)
$2160.00 (Additional Bookings from same site)

Pharmaceutical Quality Management Systems

Qualified Person & Professional Development Training

Hilton York Hotel, York, UK

4 – 8 April 2011

Designed to provide the prospective Qualified Person or any pharmaceutical professional with all they need to know to be able to design, implement, monitor and maintain a cost-effective quality management system to current international regulatory requirements.

Course Fee: **£3200.00 plus VAT** (First Booking)
£2560.00 plus VAT (Additional Bookings from same site)

Analytical Methods: Documentation, Validation & Transfer

Manchester Marriott Victoria & Albert Hotel, Manchester, UK

5 April 2011

This course will provide you with current best industry practice on how to document, validate and transfer a wide variety of analytical methods effectively and in compliance with all regulatory requirements. Come and learn from the best!

Course Fee: **£695.00 plus VAT** (First Booking)
£556.00 plus VAT (Additional Bookings from same site)

Investigating Out of Specification Results

Manchester Marriott Victoria & Albert Hotel, Manchester, UK

6 April 2011

Practical advice on how to develop, implement and operate procedures and practices which will meet the latest US and EU regulatory requirements for identifying, investigating and acting on out of specification (OOS) and out of trend (OOT) results.

Course Fee: **£695.00 plus VAT** (First Booking)
£556.00 plus VAT (Additional Bookings from same site)

Ongoing Stability Testing

Manchester Marriott Victoria & Albert Hotel, Manchester, UK

7 April 2011

The best available advice on how to design, implement, operate and manage systems and procedures for ongoing stability testing, plus essential information on how to analyse data and determine shelf life.

Course Fee: **£695.00 plus VAT** (First Booking)
£556.00 plus VAT (Additional Bookings from same site)

Workshop on Best Practices for Deviation Investigations and Best Practices for CAPA Management

Royal Sonesta Hotel, Boston, MA, USA

7 April 2011

Best Practices for Deviation Investigations – Morning 08:30-12:00
This short course will review key requirements for handling GMP investigations in pharmaceutical and biopharmaceutical operations including deviations. The scope of most systems is all encompassing; therefore well designed systems can ensure time is devoted to the most important and sensitive investigations. You will learn from someone who has interfaced with the FDA on a wide variety of difficult investigations.

Best Practices for CAPA Management – Afternoon 13:00-16:30
CAPA systems can overwhelm a facility if not well managed. This course will review key components of a well managed CAPA system. System weakness will be reviewed along with measures which will tell you whether your CAPA system is functioning for company benefit. Regulatory expectations for CAPA systems are highlighted.

Course Fee: **Half Day $300.00** **Full Day $500.00**

Achieve Operational Excellence: How to Simplify and Improve Your Batch Record Review Process

Manchester Marriott Victoria & Albert Hotel, Manchester, UK

11 – 12 April 2011

This focused, two-day course will show you how to make your batch record review process effective and value-adding, not just time-consuming. We will show you how to organise the batch disposition/ product release process for maximum effectiveness and security.

Course Fee: **£1320.00 plus VAT** (First Booking)
£1056.00 plus VAT (Additional Bookings from same site)

Achieve Operational Excellence: KPIs and Performance Measures for Quality Systems

Manchester Marriott Victoria & Albert Hotel, Manchester, UK

13 –14 April 2011

This course will help you to set effective KPIs and performance measures for your Quality Management System and will teach you how to review,, interpret and act upon them to maintain a world class quality system with maximum assurance of product quality and safety.

Course Fee: **£1320.00 plus VAT** (First Booking)
£1056.00 plus VAT (Additional Bookings from same site)

Book online at www.nsf-dba.com

Course details and prices are correct at the time of printing and are published in good faith. NSF-DBA reserves the right to make any change which may become necessary.

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Industry News

EU News

Revision of EU GMP Part 1, Chapter 5 (Production)

In November 2010 the Commission published a draft revision to Chapter 5 of the EU GMP Guide. The revisions were stated as being *"to sections 25 and 26 on the qualification of suppliers of starting material in order to reflect the legal obligation of manufacturing authorisation holders to ensure that active substances are produced in accordance with GMP. Supply chain traceability for starting materials is also introduced in sections 26 and 27. A new section, 31, is proposed in order to clarify and harmonise expectations of manufacturers regarding the testing of starting materials. Further work on chapter 5 is ongoing, affecting section 19 (i.e. regarding the need for dedicated facilities), as referred to in the Concept Papers published by EMA in February 2005."*

In essence the changes require medicinal product manufacturers to have a supplier management programme for all their starting materials. This programme must start with a process for selection and approval of suppliers and then continue with an ongoing review process. It states that for APIs, where possible, these should be purchased "directly from the manufacturer of the starting material".

Section 27 requires that *"Verification of the supply chain traceability should also be established and documented"*. This provides the basis for the supply chain 'pedigree' requirements that have been proposed in the UK by the MHRA (see later notes).

Revision of EU GMP Part 1, Chapter 7 (Contract Manufacture and Analysis)

In November 2010 the European Commission published a draft revision to this chapter. The title of this chapter has been changed to 'Outsourced Activities', broadening it from just contract manufacture and analysis to cover any outsourced activity that, if performed in house, would normally be subject to inspection. Comments on the draft should be submitted by 28 February 2011.

This revision is in response to global concerns regarding complex supply chains giving rise to risks of counterfeiting, adulteration (e.g. with Heparin) and other serious quality problems.

The principles of ICH Q10, Pharmaceutical Quality Systems, have been incorporated in this chapter consistent with the incorporation of these principles in other revised Chapters and Annexes of the EU GMP Guide.

The new section 7.7 states *"The Contract Giver should be responsible for reviewing and assessing the records and results related to the outsourced activities"*. This may prove problematic for some 'virtual' companies who currently may rely on the Contract Acceptor to review and release product.

Post-approval Change Management Protocols

The EMA published a draft list of questions and answers on post-approval change management protocols in October 2010. Post-approval change management protocols were introduced in Regulation 1234/2008. The Q&A is meant to outline general principles for using and implementing the protocols.

The document defines a post-approval change management protocol as *"specific changes that a company would like to implement during the lifecycle of the product and how these would be prepared and verified"*. The protocol is meant to take a *"stepwise approach"* including early and later evaluation of key data about the post-approval product change.

According to the document, drug manufacturers should submit to EMA as part of a marketing authorisation application (or as a stand-alone variation) the relevant data needed to demonstrate that they have *"acquired adequate knowledge to prepare and manage the impact of the change"*. For example, the protocol may include a risk assessment of the effect of the change on product quality and a description of the studies to be performed to assess the effect of the proposed change on product quality. Other examples are included in the draft Q&A.

The Q&A also discusses how and when the change should be implemented after EMA approves the protocol and what types of changes apply. The document notes that the types of changes to include in this submission would *"depend on the complexity of the product and its manufacturing process, as well as the understanding that the company has gained about them"*. The Q&A goes on to say *"it is strongly recommended that companies submit post-approval change management protocols only for those changes that they are highly likely to implement and whose feasibility has already been investigated and is supported by relevant data"*.

Finally, the draft document addresses how to handle multiple changes and the logistics of submitting information to EMA. Comments on the draft are due by 28 February 2011.

International Inspection Rationalisation Pilot Scheme

This scheme has seen the EMA collaborate with the US FDA and Australia's TGA. In November 2010 the EMA said that the 12 month API plant joint inspection programme had fostered greater collaboration between international drug industry regulators and cut the number of duplicate visits. This, in spite of the fact that, as revealed in an interim report published in October 2010, to date only seven joint inspections have been completed.

In addition at least ten duplicate inspections have taken place despite the fact that the avoidance of such wasted regulatory effort was a driver for both the development of the project in the first place and one of the metrics identified early on as a way of measuring its success.

EMA spokeswoman, Sabine Haubenreisser, said the project's aim was to boost cross border collaboration as well as to increase the number of joint inspections and *"The project has been a success, much media attention seems to be given to the joint inspection activity overlooking the other equally important parts of the project"*.

The interim report's wider conclusions highlight the 1,046 separate inspections that have been carried out and an increase in the level of information exchanged as key achievements and indicators of progress.

Dr Haubenreisser also said that while some sites had been assessed more than once *"it is self evident that a number of duplicate inspections have been avoided through either a joint inspection or the sharing of reports. We are in the process of looking at lessons learned by reviewing feedback provided by the partners. The EMA has noted that there is a need for an improved shared inventory of sites of common interest and supporting software applications and a need for longer planning lead times to arrange joint inspections"*.

The 12 month pilot scheme was due to finish at the end of 2010 and, according to Haubenreisser, *"a final report will be published thereafter in the first quarter of 2011"*.

ICH News

Global Co-operation Group

The International Conference on Harmonization (ICH) Steering Committee (SC) met in Fukuoka, Japan, during 6-11 November 2010. At this meeting they agreed that ICH will move to open further technical collaboration with non-ICH regions.

The ICH SC endorsed opening the ICH technical working groups to qualifying members of the Global Co-operation Group (GCG). The GCG includes representatives from Australia, Brazil, China, Chinese Taipei, India, Russia, South Korea and Singapore, as well the Asia-Pacific Economic Co-operation (APEC), the Association of Southeast Asian Nations (ASEAN), Gulf Co-operation Countries (GCC), the Pan American Network on Drug Regulatory Harmonization (PANDRH) and the Southern African Development Community (SADC). This represents a new level of involvement of the GCG and will provide an opportunity for direct technical contributions to the work of ICH, a more global perspective, and will advance implementation of ICH guidelines.

Industry News

WHO News

WHO Quality Risk Management Draft Guideline

In August 2010 WHO made public draft guidelines on Quality Risk Management. The draft represents a move away from the hazard analysis and critical control point (HACCP) methodology previously recommended by WHO, in favour of the risk management principles outlined by ICH Q9.

This is a detailed guide that builds on the framework given in ICH Q9 and is far more useful than the dreadful PIC/S draft that was published in January 2010. Given that WHO guidance is often utilised by developing countries it is somewhat difficult to see this detailed guide being widely implemented in those areas. It is, however, likely to be taken up by regulatory authorities in the first world. The organisation and contents of this draft WHO guide are as follows:

Chapter 1 is an introduction and describes the current WHO approach to QRM, which is now based on ICH Q9. The text emphasises the fact that risk management modules other than the one described in ICH Q9 can also be applied. WHO adds two additional principles of QRM to the two given in Q9:

- QRM should be dynamic, iterative and responsive to change
- The capability for continual improvement and enhancement should be embedded in the QRM process

WHO points out that there are connections to GCP and GLP.

Chapter 2 is interesting in that it describes QRM considerations for regulatory authorities. Section 2.2.1 includes a checklist for inspecting QRM and 2.2.2 lays down the inspection of risk-based decisions.

Chapter 3 includes requirements on QRM for pharmaceutical manufacturers. There are detailed specifications regarding:

- Training and education
- Roles and responsibilities
- Initiating a QRM process (which includes a specific requirement to construct and confirm a flow diagram)
- Conducting a risk assessment
- Risk control
- Risk communication and documentation
- Risk monitoring and review
- Corrective actions
- Verification of a QRM plan

Separate parts of chapter 3 are dedicated to the application of QRM in product development and during validation/qualification. The guideline refers to the FDA draft guidance on process validation.

Chapter 4 is on 'Risk Management Tools' and Chapter 5 contains a glossary. Chapter 6 contains references and includes a reference to the MHRA's Q&A paper on QRM (some parts of the draft guide appear to be direct quotes from the MHRA Q&A). Like the MHRA paper, the WHO draft requires a 'risk register' to be maintained.

This draft document may still be changed before being formally adopted by WHO.

PIC/S News

At its last meeting in Kuala Lumpur (Malaysia) on 8-9 November 2010, the PIC/S Committee invited the US Food and Drug Administration (FDA) and the Ukraine's State Inspectorate for Quality Control of Medicines (SIQCM) to join the Pharmaceutical Inspection Co-operation Scheme as from 1 January 2011.

The FDA will become PIC/S' 38th Participating Authority while SIQCM will become the 39th Participating Authority.

NSF-DBA launch a ground breaking work-based Diploma for the Medical Device Industry

As part of our continuous programme of developing the services offered by NSF-DBA, during this, our 25th anniversary year, we will be introducing a brand new Medical Devices Diploma.

After 18 months of development and a major survey of medical device quality and regulatory learning needs we have formulated a body of knowledge that has identified all of the major aspects of becoming an effective professional in medical device regulations.

The Diploma itself offers eight core modules to provide the modern medical device professional with the knowledge, tools and techniques needed to manage the many aspects of worldwide medical device quality management and regulatory affairs.

The Diploma Process

The NSF-DBA Diploma uses blended learning techniques to ensure that the students' experience is enhanced. The approach of the NSF-DBA Diploma suits all learning styles and will ensure that students are effective in their understanding whilst completing the Diploma.

The Diploma includes:

- Workbooks
- Case studies
- Exercises
- Knowledge tests
- Key learning points
- Podcasts
- Visual diagrams of models and flowcharts
- Video clips
- Online reference library
- Online tutor support

All course content is available online through a student portal and includes access to references, templates, case studies, podcasts and video resources.

The benefits of the Diploma are:

- Integrated work based projects and assignments with tutor feedback that will enhance the learning experience and enable the candidate to study whilst at work
- Access to a dedicated medical devices tutor throughout their education
- Practical, challenging and innovative workbook learning methods
- Accreditation of prior learning for those who have previously studied recognised and relevant courses
- Up-to-date application of the most current and effective thinking for medical devices
- A formal industry recognised certificate
- Excellent professional recognition

The Diploma will demonstrate the candidates' practical achievement of competence in the application of quality and regulatory practice within the medical device industry.

The Diploma Core Modules are:

Module 1	Medical Device Regulatory Frameworks
Module 2	Medical Device Risk Management Design Development and Product Validation
Module 3	Medical Device Clinical Evaluation
Module 4	Medical Device Conformity Assessment – Preparing and Managing Technical Documentation
Module 5	Medical Device Conformity Assessment – Implementing and Managing Quality Management System Processes
Module 6	Medical Device Post-Market Surveillance and Vigilance
Module 7	Working with Competent Authorities, Notified Bodies and other Regulatory Stakeholders
Module 8	Management and Behavioural Skills in Quality Assurance and Regulatory Affairs

When developing the Diploma it was important to us that the previous knowledge and experience of students are taken into account as an accreditation of prior learning, thus enabling them to concentrate on demonstrating their competence through the assignments and projects.

When applying for the Diploma, candidates will be required to identify any specific training that they believe may support their fundamental knowledge of the learning outcomes. We will then evaluate this information and work with them to determine their route to successful completion of the Diploma.

We have created a specific model for reviewing all candidates' existing in-house and/or external training to determine whether or not they qualify for exemptions to any of the above modules.

Progressing through the Diploma will enhance their technical and management skills and can be used for their own professional development as well as creating considerable benefits to their organisation.

To enrol for the Diploma or to find out more contact us at jp@nsf-dba.co.uk

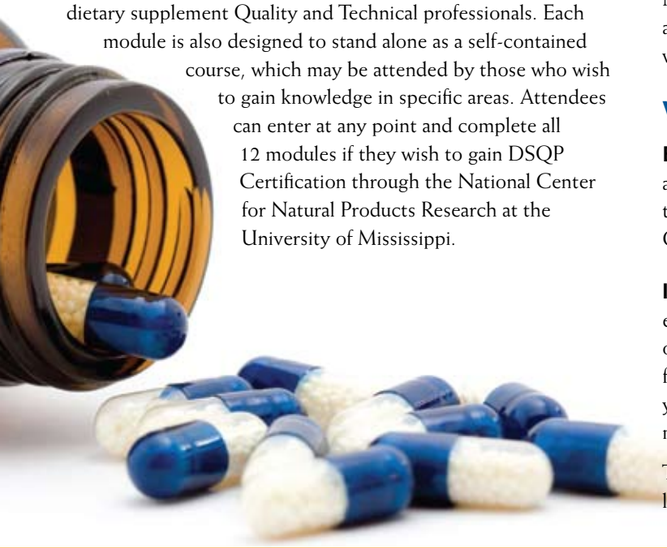
NSF-DBA launches educational program for dietary supplements industry professionals

Casey Coy describes this important new initiative

We are proud to announce the launch of a ground-breaking program of structured educational classes designed specifically to provide Quality and Regulatory professionals in the dietary supplements industry with the knowledge and skills they need to be able to face the challenges ahead and to perform their roles effectively and with professionalism.

Building upon our international reputation for providing outstanding educational programs for industry professionals (Qualified Person training in Europe, the Quality Leadership Program in the US and the newly launched Medical Devices Diploma), we have partnered with the National Center for Natural Products Research (NCPR) at the University of Mississippi and the United Natural Products Association to deliver a series of educational and professional development classes for this relatively recently regulated industry sector. We have called the series the Dietary Supplements Quality Professional Certification Program (DSQP).

The DSQP educational program consists of a series of 12 modules offered over a one year period. Together, they are designed to provide the knowledge and skills required of today's dietary supplement Quality and Technical professionals. Each module is also designed to stand alone as a self-contained course, which may be attended by those who wish to gain knowledge in specific areas. Attendees can enter at any point and complete all 12 modules if they wish to gain DSQP Certification through the National Center for Natural Products Research at the University of Mississippi.



The module series includes:

- 21 CFR 111 – GMP Overview
- SOP and Record Keeping for Compliance to 21 CFR 111
- FDA Inspection Readiness
- CAPA (Corrective Action) Management
- Testing Method Selection, Specification Setting and Equipment Qualification
- Stability Program Development
- Vendor Qualification and Audit Training
- Cleaning and Control of Cross-contamination
- Process Definition and Control; Facility/Utilities Design and Monitoring
- Risk Assessment and Risk Management
- Staff Recruitment and Internal Training Development
- International Regulatory Requirements for Dietary Supplements

Partnerships

NSF-DBA's partnerships with the National Center for Natural Products Research at the University of Mississippi and the United Natural Products Alliance involves review of the course materials and the provision of an official DSQP Certification to individuals who complete the program by the University of Mississippi.

Venue and Format

External Program – NSF-DBA is pleased to announce the availability of this program beginning in February 2011 with training offered in Ann Arbor, Michigan, Salt Lake City, Utah and Oxford, Mississippi.

In-House Program – NSF-DBA encourages companies to consider bringing organized instruction in-house, as this allows for customization and team-building within your company. Please contact Casey Coy for more details.

The chart opposite outlines the dates and locations of our 2011 Training Calendar.

Casey Coy

2011 Dates	Course Title	Location	Duration
February 8-9	**21 CFR 111 Dietary Supplement GMP Overview**	Salt Lake City, Utah	2 days
February 10	**SOP and Record Keeping for Compliance to 21 CFR 111**	Salt Lake City, Utah	1 day
February 22	**FDA Inspection Readiness**	NSF International HQ, Ann Arbor, MI	1 day
February 23	**Corrective Action and Management (CAPA)**	NSF International HQ, Ann Arbor, MI	1 day
March 15	**FDA Inspection Readiness**	Salt Lake City, Utah	1 day
March 16	**Corrective Action and Management (CAPA)**	Salt Lake City, Utah	1 day
April 5-7	**Testing Method Selection, Specification Setting and Equipment Qualification**	NSF International HQ, Ann Arbor, MI	3 days
May 2-3	**Vendor Qualification and Audit Training**	Secaucus, NJ prior to SupplySide East	2 days
May 24	**Cleaning and Control of Cross-Contamination**	NSF International HQ, Ann Arbor, MI	1 day
May 25	**Process Definition and Control; Facility/Utilities Design and Monitoring**	NSF International HQ, Ann Arbor, MI	1 day
June 7-8	**21 CFR 111 Dietary Supplement GMP Overview**	NSF International HQ, Ann Arbor, MI	2 days
June 9	**SOP and Record Keeping for Compliance to 21 CFR 111**	NSF International HQ, Ann Arbor, MI	1 day
July 12-14	**Testing Method Selection, Specification Setting and Equipment Qualification**	NCNPR Ole Miss	3 days
July 19	**Cleaning and Control of Cross-Contamination**	Salt Lake City, Utah	1 day
July 20	**Process Definition and Control; Facility/Utilities Design and Monitoring**	Salt Lake City, Utah	1 day
September 6-7	**Risk Assessment and Risk Management**	NCNPR at University of Mississippi in Oxford, MS	2 days
September 20-22	**Staff Recruitment and Internal Training Development**	NCNPR at University of Mississippi in Oxford, MS	3 days
October 11-12	**Stability Program Development**	Las Vegas, NV prior to SupplySide West	2 days
October 18-19	**International Regulatory Requirements for DS**	Salt Lake City, Utah	2 days
November 8-9	**International Regulatory Requirements for DS**	NSF International HQ, Ann Arbor, MI	2 days

For more information, or to enroll, contact Casey Coy at NSF-DBA, 734-913-5734, toll-free at 800.NSF.MARK (673-6275) extension 5734 or email coy@nsf.org

Quality, Operational Excellence and Continual Improvement in the Pharmaceutical/Biotechnology Industry

Introduction/Background

It is well documented that the pharmaceutical/biotechnology industry has lagged behind other industries in its approach to quality, operational excellence and continual improvement.

From the late 1990s through to the mid 2000s, a range of independent reports (PWC/IBM) as well as headlines in the Wall Street Journal continued to draw conclusions that the industry:

1) Was highly inefficient in its development and manufacturing processes, with high levels of waste/rejects, an absence of understanding of processes and their capabilities, and a lack of progress in embracing new technologies.
2) Relied heavily on a quality control approach, with resulting high costs of compliance, but did not measure the real cost of quality in any systematic way.
3) Did not embrace quality improvement philosophies/tools/techniques – initiatives such as lean/Six Sigma, etc, were not seen as quality improvements/processes, rather something separate, often seen as a project rather than a culture.

Throughout the late 1990s/early 2000s the above findings catalyzed meaningful and beneficial discussions between the regulators, especially FDA and industry, to get to the bottom of how the industry can improve. What emerged from these collaborations was an acknowledgement that both the regulators and industry had to play strong roles and work together to break away from what had become the 'status quo'.

Discussions between FDA and industry led to initiatives such as FDA's cGMP for the 21st Century (which was much broader than just GMP) and the delivery of the ICH guidelines Q8/9/10 – all seeking a modernization of pharma with a strong focus to bring about a science and risk-based culture, leading to a true lifecycle approach, higher product and process understanding, more efficient product manufacturing and an ability to make improvements/innovations, all ultimately with a focus on the patient.

We therefore have the key to unlocking the culture change needed to improve.

During this period of time the pressures on the pharmaceutical/biotechnology industry continued to increase dramatically. The focus turned to survival and seeking competitive advantage wherever possible.

R&D and marketing had increased expenditure, but were not delivering the revenues promised. At the same time factors such as Government pricing initiatives, fierce generic competition and lower cost alternatives have eroded traditional margins and made the need to drive out inefficiencies/reduce operating costs unavoidable – so under these pressures, are we now embracing the challenge to improve?

Are we taking the opportunities to build sustainable ways of developing/supplying medicines and reducing the cost of goods sold (COGS)?… or are we fixed on the short term with short-sighted cost saving measures?

2010 Report Card

Let's look closer at what happened in 2010. If the 2005 IBM report was re-issued, what would it say? NSF-DBA sees a variety of companies in our work. Within this variety we see a wide cross-section of reactions to the current industry climate, ranging from forward thinking proactive firms who see the need to change culture, embrace Q8/9/10 thinking and drive improvement within their organization/facilities, to those who continue to disappear under the weight of issues/unresolved investigations, generate more SOPs/complexity and lurch from one inspection or warning letter to the next, hoping to avoid greater sanctions.

These firms then have no choice but to spend large amounts of money when under consent decrees, and then they somehow always seem to find the resources needed.

One thing is for certain, the pharmaceutical industry does not move quickly, and unfortunately many firms often wait until the regulators tell them what to do rather than take a proactive approach. This is often a characteristic of firms that do end up in trouble with the regulators.

In our experiences of working with proactive firms, moving forward requires strong leadership that embraces a highly visible quality culture and seeks to embed this cross-functionally throughout their organizations. We also see many senior leaders, sadly including some heads of quality, who only see short-term compliance and 'keeping out of trouble' as their 'raison d'etre', rather than driving improvement and contributing to business performance.

Separate Quality – Not the Answer

Pharma is the only industry, to my knowledge, that legally demands a separate independent quality unit. Whilst the original aim was a noble one, it can also drive inappropriate behavior by dumping all quality issues with the quality unit and creating an 'us vs them' (good guy/bad guy) culture. Behaviors do not always align with the fact that quality is everybody's responsibility.

This also manifests itself where companies have undertaken lean or Six Sigma type operational excellence activities. The concepts of Q8/9/10 fit 'hand in glove' with operational excellence, yet we often see such initiatives run as discrete projects (rather than long-term culture changes), often run by 'elite' groups in isolation from the quality unit/other technical areas. An issue we often see at firms is that anything with 'lean' or 'OpEx' in the title gets approved by senior management, whereas those within 'quality' or 'improvement' are questioned harder. A more holistic view of how these fit together is often lacking.

All these would sit integrated under a single continual improvement umbrella in other industry sectors – so why not us? I'm pleased to say a few leading pharmaceutical/ biotechnology firms have recognized/are recognizing this at last with a more holistic overall approach to improvement.

The concepts of product and process understanding, process capability, statistical process control, real time release, quality performance indicators, cost of quality, management review, etc have finally now found their way into pharmaceutical guidance and regulatory expectations, having been the norm in other industry sectors for many years.

Two to three years ago very few firms we were working with were actually embedding these concepts into routine activities and pharmaceutical quality systems. Today the numbers are increasing, but still many firms are not on-board, or just waiting to be told to do it. So, despite some leaders, the industry overall is still only at an early stage of implementing the performance improvements.

Sadly, there are also some who believe it will all go away, with public health issues driving the regulators to more stringent enforcement – so why bother? The challenge here for the regulators is to come down hard on the higher risk players, whilst still being seen to be supportive of those firms who are driving improvement. This is completely in line with regulators following the risk-based approaches articulated in ICH Q9.

Long-Term Cost of Quality Model is a Must

In our experiences very few pharmaceutical/biotechnology companies have a timely, effective and integrated cost of quality model working in practice – so in many cases the true costs of prevention, appraisal and failure are not being measured/are not visible to senior management. **Some firms often still see the quality unit purely as an overhead, rather than as the value-adding function an effective quality unit can be.** It is usually these firms that then chop head count in response to short term pressures without understanding, or choosing to ignore, the longer term implications.

The ISO cost of quality model shows that investment in appraisal costs may be needed before the total cost of quality will be reduced – a short-term view may not sanction this.

All too often we see the quality performance indicators measured are too many, too complex and often actually driving the wrong behaviors. For example, metrics such as 'completing an investigation in 30 days' are often driven by perceived regulatory expectation, rather than by having a really efficient and effective Corrective Action/Preventive Action (CAPA) system. Many of the quality performance indicators have been monitored for years, with no real improvement element – in some cases, no-one remembers why they are measured and who, if anyone, does anything with the data/information generated.

Improvement Still Needed

From NSF-DBA's perspective, the overall industry, despite all the current drivers to become more efficient and effective to survive, is only making relatively slow progress in the modernization of development/manufacturing and integration into the pharmaceutical quality system. We still do not yet appear to be a learning industry, with the same issues still occurring again and again.

One factor that continues to have a major impact is the high level of merger and acquisitions. The consolidation usually involves a strong expectation that early 'synergies' will be delivered. This can have the opposite impact to creating a sustainable long term improvement culture, with much effort usually focused on delivering the short term 'quick hits'. It is challenging to maintain a leadership vision during this period.

However, we do see that those companies with genuine leaders supporting quality and improvement are moving forward. Whilst their leadership is essential to embed the quality culture throughout, the organization also needs to take a bottom-up approach to complement the top-down drive.

Culture change is not a project, and will take time. To achieve the bottom-up element and develop key staff as the catalysts/enzymes for change throughout the organization/different sites/different functions, needs a good education program to broaden these key individuals. Training alone is not enough – education of WHY is crucial too…!

So the industry report card may read: "**B- to C+ could do better**"

Do you want to do better?

NSF-DBA believes that to drive modernization and embed a quality culture within a company your key individuals must be equipped with the skills and knowledge to lead change and make high quality risk-based decisions.

Our educational courses and modular programs have been developed by seasoned pharmaceutical and biotechnology experts and reflect the current global regulatory and technical requirements and expectations.

NSF-DBA has worked with a range of firms to develop and customize in-house Quality Leadership Programs to help change the quality culture and develop key personnel.

We also launched our US Quality Leadership Program (QLP) as an external program in 2009. This has the option of a Masters Degree.

Via our in-house Quality Leadership Programs or via our external Quality Leadership Program (QLP), we can help develop your key staff to impact your culture and drive improvement.

About the Author

Neil Wilkinson is a partner at NSF-DBA, based in our Boston, USA office. He spent over 25 years in the pharmaceutical industry in a range of quality, manufacturing and supply roles, including extensive international experience. He worked with both PhRMA and Efpia technical groups and within ICH was the EU industry lead on the ICH Q10 Expert Work Group. He can be contacted at **njw@nsf-dba.com**

To find out more – contact us at www.nsf-dba.com

NSF DBA℠ 25 YEARS OF EXCELLENCE

People

We are pleased to announce two new members to the NSF-DBA team

Matt Krsulich

Matt holds a Bachelor of Science in Chemistry and a Master of Science in Pharmaceutical Science. He has extensive quality management experience, having managed QC, QA, compliance and regulatory CMC projects at a senior level at Pfizer Inc. With nearly 30 years' pharmaceutical experience, Matt has detailed knowledge of global GMP requirements and diverse regulatory inspection experience. He has managed issues related to new product launches and quality systems development and implementation. He has provided quality oversight for a wide variety of manufacturing processes, including drug product intermediates, clinical supplies manufacturing/packaging and a variety of drug product formulations. Due to his insight and appreciation for key regulatory inspection issues, Matt is a highly effective pharmaceutical auditor.

Outside of work Matt is an avid sports fan and has been a coach in multiple sports. We are pleased to add Matt to our USA associate team and feel his experience will add breadth to our US operation.

Chris Harris

Chris is an industrial statistician providing consultancy and training in the field of quality improvement. He covers all of the quality disciplines: quality function deployment (QFD), design for manufacture and assembly (DFMA), value engineering (VE), failure mode and effects analysis (FMEA), fault tree analysis (FTA), design of experiments (DOE – TAGUCHI, response surface methods), statistical process control (SPC), measurement systems analysis (MSA), problem solving (8D), Six Sigma, statistical methods, reliability, auditing quality systems, critical path analysis (CPA), quality operating systems (QOS/BOS). Chris has been a consultant to the Ford Motor Company (approved trainer) and its supply base since 1982 and to the Mars Organisation since 1985. During this time many other companies, both home and abroad, and in industries such as engineering, pharmaceutical, snack foods, electronics, aerospace, pet food, packaging, chemical, vending, police, retail, finance, plastics, cement and concrete, F1 motor racing and government (Department of Social Security) have become clients. When not at work Chris is an keen Chelsea football fan and rarely misses a home game. Chris brings his wealth of practical application and understanding of statistical processes to NSF-DBA and we are pleased to welcome him to the team.

Operational Excellence at Kirkbymoorside

Have you ever wondered how one of our Journals or course brochures or training course booklets ends up on your desk or through your post box? The answer is probably not – so we thought in this Journal edition we would feature those members of our team whose role it is to make it happen!

Our quality assurance and office support teams, although small, are perfectly formed!

Before any of our externally produced documents go to print or are despatched to you, we have two team members dedicated to proof reading the content of each and every page of these publications, scanning for grammatical and spelling errors – and any other 'bloomers' which have somehow slipped in through the production process! Janet Lovering and Sally Simpson are our very own 'hawkeyes', making sure that the end product you receive is always of the highest NSF-DBA quality standard. Quality for us is not just an aspiration but the cornerstone upon which our company was founded and from which we benchmark everything we do. Janet and Sally take great pride in their roles and work to very tight deadlines most of the time, but their mission is to make sure that only quality documents leave the office.

Once approved, the documents go to print, are delivered to our offices here and are then mailed to you as part of a tightly scheduled monthly timetable. Sally's role switches from proof reader to mailing supervisor and, with her colleague Annette White, ensures that your personal copies of our various promotional materials are delivered to you within the planned timescales – wherever in the world that might be!

Sally, working again with Annette, is also responsible for ensuring that training course booklets are copied, packed and despatched to our individual client companies or external training venues. This can often be a very last-minute process, particularly if we are waiting for a delegate list, for example, or another part of the course documentation. We have three large state of the art photocopiers, often all in production at the same time, set up to produce quickly and effectively the quality delegate documentation you receive. Even following our standard secretarial checks, each booklet is given a final scan by Sally to ensure you receive a quality end product.

Whilst it may not be apparent to you and we normally portray a picture of calm and controlled efficiency, the teams often work frantically to meet deadlines, particularly if a photocopier has broken down, or some brochures are not delivered on the due date or our course material is stuck in a courier depot because of the weather conditions!

We hope you appreciate this brief insight into part of our office operations.

NSF-DBA offers its services in the Italian language

We are delighted to announce we are ready to offer a range of training and consultancy in Italy.

All this will be possible through collaboration with local consultants, selected because of their experience, ability and expertise. The project will be led for us by our new associate Giovanni Cosmi.

Giovanni is very fond of rugby and has never missed any domestic match of the 6 Nations since 2000. He also has a passion for listening to jazz music while travelling and while at home.

He also likes to cook for his family and friends – good food should always be served with good wine!

Giovanni has over 20 years' experience in the Italian pharmaceutical industry, most recently with Pfizer, also with Bristol-Myers Squibb. He has held senior positions in QC, QA and Project Management and so he brings to us a wealth of knowledge of both strategic planning and day to day application of GMP in the EU regulatory framework.

We believe that by providing local experts who can communicate in Italian, and integrate with the client, understanding their needs, listening to their problems and building good relationships, will enable us to provide a more efficient and effective service, allowing the client to benefit fully from the expertise we have to offer.

At the end of 2010 we reached out to our Italian clients informing them that we were preparing the first training programmes in Italy, using local trainers and language.

So they do not have to be able to speak English to benefit from the services we have to offer.

At the same time we requested that they indicate their training topic priorities so that we can include them in future tailored programmes for the Italian pharmaceutical industry. We believe that to know and understand the needs of our clients will help NSF-DBA work closely with them to ensure we deliver just what they want.

We propose to launch our venture with programmes in Milan in 2011.

Later programmes will be offered that represent the customer survey results. All our programmes can be found on our website and we will continue to keep our Italian customers updated with postal flyers.

This new venture is both challenging and exciting for us at NSF-DBA. We welcome Giovanni to the team and we look forward to meeting our customers soon in Milan.

All our programmes can be found on our website: www.nsf-dba.com

Charity begins at our home

If you work at NSF-DBA then you really have to have a charitable disposition, and that is not because the Partners are needy! The staff at the Kirkbymoorside office are very generous with their time and efforts and are always pulling together to collect money for one or another charity event. Here are some of the highlights for 2010 (that have not already been featured in our journals already).

NSF-DBA's newest recruit, Gill Gibbeson, has been working with NSF-DBA on a temporary contract and will now join the permanent staff in 2011 (we are all pleased to welcome her to the team). Gill regularly organises us with fun ideas for raising money. In 2010, we played 'Ducky Ducks' and joined the 'Wear Pink' day (surprisingly suits Martin!) and with her help we have collected over £100 for **Cancer Research, Breast Cancer Awareness and Marie Curie Cancer Care.**

Jill Aveyard is secretary to Peter Gough. In 2008 she tragically lost her 11 year old niece. In her memory and with family and friends, they decided to raise funds for a charity called **Well Child**. This charity helps families to cope with sick or recovering children. They provide nursing help to parents. The group sets a target to provide funds for one nurse to be available for family support for one year. Their efforts, which included bag packing at the local supermarket, meant that two nurses would be available in 2010. Well done Jill.

Claire Bettany can usually be seen running for local charity events, this year while returning to fitness after a maternity break she rallied the troops for a **Jeans for Genes** day. She is now training to get back on the charity runs.

NSF-DBA is keen to show support for both local and international good causes. We all know that Martin Lush likes to keep fit running and cycling, but he is also a regular organiser of the Kirkbymoorside 10K. This event is sponsored by NSF-DBA and has now been going for 10 years. In that time the event has raised an amazing £15,000 for nominated charities. Also when earlier this year the world witnessed the tragic events unfold in Haiti, and we all wanted to do something to help, NSF-DBA vowed to contribute 1% of its turnover in January and February to the cause and were pleased to send a cheque in early March to support the hard work being done for those badly affected.

Charity work can be fun and provide a chance to combine our passions. Sally Simpson is lucky enough to own a TEF20 Ferguson tractor in grey (called Bert). Twice a year Sally helps to organise a fun event involving lots of other tractor enthusiasts. Around 100 tractors follow a route through the North Yorkshire villages, collecting money with buckets and providing time for people to sit, ride and generally admire the tractors. In 2010 they raised money for **Yorkshire Air Ambulance and Marie Curie Cancer Care**.

There have been other runs, collections and events already mentioned in our 2010 journals and so thanks to all who support the efforts of our team, because in our house in Kirkbymoorside charity really does begin at home!

In the next NSF-DBA Journal:

Industry News: As ever we search for regulatory changes so you don't have to; Tech Talk: Providing the usual NSF-DBA thought-provoking opinions; DBA People: Exciting new additions to our team to enhance our services worldwide; Forthcoming Courses: A review of our education programmes for 2011; Plus: All the latest news for Qualified Persons and Technical Professionals in the field of pharmaceuticals, medical devices and nutraceuticals.

If you have any comments or suggestions for the next issue of the Journal, please email us at journal@nsf-dba.com

NSF-DBA

Europe The Georgian House, 22-24 West End, Kirkbymoorside, York, UK, YO62 6AF
Tel: +44 (0)1751 432999 Fax: +44 (0)1751 432450 Email: mail@nsf-dba.com

USA Suite 19, 101 Federal St., Boston, MA 02110, USA
Tel: 617-342 3625 Fax: 617-342 3623 Email: USinfo@nsf-dba.com

www.nsf-dba.com