

DBA

The Journal of David Begg Associates

Issue 14 Winter 2009/10

Managing Quality

what can Toyota teach the healthcare industry?

Combination Products

does a new category of products require a new approach to quality management?

Is it time to throw away your remote particle counting system?

welcome



Bob Pietrowski,
Managing Partner
David Begg
Associates

Wishing you a happy and successful 2010

As we enter a new year, I'm sure we all hope for better things, better economic prospects for ourselves and our employers, more opportunities to progress in our careers and perhaps greater resilience to face the challenges ahead. On behalf of everyone at DBA, may I wish you health, happiness and success in the coming year.

The new year is also an opportunity to look back at the year just gone. 2009 has not been an easy year for any of us, but hard work and attention to what really matters has seen us all through. We have become adept at doing more with less and we are all more experienced at using risk assessment to define priorities. These skills will be of great value to use in the months and years ahead.

2009 has been a year of achievement for DBA. We have grown our North American business significantly over the year and have launched our flagship Quality Leadership educational program to great acclaim (see page 14). Perhaps most encouraging for us is that in-house training in Europe grew by an amazing 70%! We want to thank you most sincerely for putting your faith in us during such difficult times.

Be sure that we at DBA will do all in our power to continue to repay the trust you put in us. At the same time, we will be doing all we can to enhance and expand our services to you in two relatively new sectors for us: medical devices and dietary supplements.

Whatever your discipline, whatever your needs, DBA is here to help

A handwritten signature in white ink that reads "Bob Pietrowski". The signature is written in a cursive style and is underlined with a single horizontal stroke.

Bob Pietrowski
Managing Partner

DBA
The Pharmaceutical
Training Specialists

Tech Talk



Combination Products – does a new category of products require a new approach to Quality Management?

Christa Hartmann, Director, Corporate Quality, Genentech Inc., USA, argues for a holistic approach

How should a company approach the Quality System when thinking of entering into the combination product world or if they're already involved in the manufacture of combination products? One can think of creating a quality system for combination products in several different ways, so let's begin with the following scenario of the three little VPs of Quality.

Three VPs of Quality are sitting in a room together and the first VP says, "Well, I'm a drug manufacturer and I think the quality system is robust enough by following Parts 210/211 so I'm just going to have a Quality System focused on those regulations." And the result of this decision is you are building your quality system on a foundation of straw. But then another VP of Quality who's in the room says, "Well, I'm a medical device manufacturer and I think Part 820 is the most up-to-date, robust quality system regulation so I'm going to ignore Part 210/211 and I'm going to stay with what I know." The result of that decision is that you build your Quality System on a foundation of sticks. Finally, the third VP says, "Well, I've been involved with making combination products and I have enough experience to know that there are parts of 210/211 and parts of 820 that are good and if I combined them, I would have a quality system that was the best in class, and so I'm going to take both of these regulations and therefore my foundation for the Quality System is built on a foundation of stone."

Now, let's ask the question: who is the big, bad wolf in this three little VPs scenario? Some people would say that it would be the regulators. However, the big, bad wolf is actually the company's reputation because if you don't take into consideration all of the strengths of both regulations, then you might manufacture a product, release it to the market, and if it hasn't been manufactured in a robust fashion, you might lose your reputation in the marketplace due to product quality issues.

What do we know from the FDA? Recently, the proposed rule came out for GMPs for combination products. For co-packaged or single-entity combination products, where the manufacturer's quality system has been shown to comply with drug GMPs, the following quality system regulation requirements must also be met from Part 820: management review, design controls, purchasing controls, corrective and preventive action, and where applicable, installation and servicing.

Why should a company think about Part 820? Our company manufactures combination products and has traditionally built its Quality System around the drug regulation and has gradually added selected elements of Part 820. There are multiple angles of attack for redesigning a Quality System all aimed by using a systematic approach. Our company embarked on a complete Quality System redesign in 2007, where we performed gap assessments and remediation against both 21 CFR Part 820 and ISO 13485. We also looked at introducing elements of ICH Q8, Q9 and Q10, and then as part of this system redesign, we did business process mapping and optimization before we redesigned the quality system. We had some thoughts on where we wanted to evolve our Quality System – we wanted to go from:

- relying on compliance to a system that is integrated into the overall business processes
- controlling and reactive to planning, proactive and confirmatory
- discrete activities to continuous monitoring and improvement
- site and local manufacturing to a company that is global
- mechanical to a risk and knowledge-based quality system
- training our staff to education
- a focus on SOPs to supplying adequate tools to the people that need to interact with the Quality System

Tech Talk

Our new Quality System is based on regulatory expectations with a focus on the structure as dictated by ICH Q10 where the four subsystems are management responsibility, system elements, operations, and enablers. The document hierarchy in our system has the quality policy followed by quality requirements and global standards and then other supporting documentation.

What have the challenges been during design and implementation of this new system? Why is it so hard to do a Quality System redesign? When we looked at it, ICH Q8, 9 and 10, as well as the rest of world regulations, were not fully incorporated into our previously existing Quality System. What makes it challenging is that when you introduce new requirements, you have to think about human change management. What this looks like is that people may say, "Well, I've been inspected multiple times by the regulators and I have never been given an observation; why are you making me change my processes and why does it matter if they are not consistent across all manufacturing sites? We also realized that Part 820 was not fully covered in the existing Quality System which, combined with little formal regulatory guidance for combination products, resulted in another opportunity to educate our product development and Quality personnel.

As mentioned earlier, we have some experience developing combination products, but initially we weren't very familiar with the iterative nature of design controls. We realized at the end of the day that the first prototype is **not** perfect. If you develop your first device prototype for your combination product and decide that's the design going to market, you could experience delaying introduction into the market due to design problems you hadn't planned or anticipated. We also initially didn't take into consideration the potential for manufacturability issues at

component manufacturers, so insure that the selection process is robust and that the responsibilities of the device manufacturer are clear. There also was an inadequate understanding that development ends at design freeze and were challenged with how to handle design changes after design freeze. We learned that the main difference between 21 CFR 211 and 820 is that with Part 820, the Quality System is the sum of all the parts and not just functions or things one must have or do in the system – all of the parts of the Quality System must communicate with each other.

What are our next steps? We are focusing on completing the implementation of Part 820. In most cases, we were already doing the right thing, but it wasn't fully integrated or understood as part of the quality system. We have identified quality system gaps and we have recommended remediation in place.

Why use this approach? What are the business benefits? First, there's simplification of major systems across the organization by using a lifecycle approach with one process to fit all product types wherever possible. It makes it a lot easier to execute design and development of products. There is also an overall reduction in quality system documentation because of the elimination of redundant and conflicting procedures. Also, through harmonization, with several to many manufacturing sites, you shouldn't have five different procedures for all the elements in your quality system. You should realize that the company is seen as one by authorities, patients and stakeholders then you should have just one quality system – it actually makes the inspection process by the regulators that much more simple. It increases the flexibility process for continual improvement and creates more consistent guidance for the organization. So what we envisioned was an integrated holistic approach to the quality system, and if given the opportunity to build or redesign your quality system with a solid foundation from the best source material why wouldn't you do it?



DBA

Medical Devices



Our Portfolio of Medical Devices Training Courses...

Over the last few months, we have worked hard to pull together a portfolio of training courses for the medical devices industry. This portfolio has been largely designed by you, our clients, following discussions on what you feel you need.

We are now able to offer the following training courses to help you develop your staff...

Regulatory Series

- Understanding the European Medical Device Regulations and the Latest Updates
- Implementing the Medical Device Directive 93/42/EEC for Active and Software Based Devices
- Implementing the Medical Device Directive 93/42/EEC for General and Implantable Medical Devices
- Post Market Surveillance and Vigilance Requirements for Medical Devices
- Managing Worldwide Registration for Medical Devices

Design and Technical Series

- Design, Development and Performance Evaluation for General Non-Active and Implantable Medical Devices
- Design, Development and Performance Evaluation for Active and Software Based Medical Devices

Auditor Series

- Medical Devices Internal Quality Auditor Training
- Supplier Quality Auditing for Medical Devices

Quality Series

- Understanding ISO 13485:2003 and Worldwide Quality Management System for Medical Devices
- Implementing ISO 13485:2003 and Worldwide Quality Management Systems for Medical Devices
- Implementing ISO 14971:2007
- Supplier Evaluation, Qualification and Control for Medical Devices
- Managing Corporate Global Quality and Regulatory Strategies
- Understanding Process Validation for Medical Devices
- Implementing Process Validation for Medical Devices
- Process Validation Masterclass for Experienced Validation Staff



Many of these will be offered via residential courses in 2010. A dedicated Medical Device Training Programme will be published and mailed to you shortly.

However, all these courses are available as in-house classes right now!

If you would like to discuss your medical devices training needs, why not email us or call us. We are here to help you.

Forthcoming Courses

What's planned for the first four months of 2010

Pharmaceutical Packaging

Qualified Person & Professional
Development Training



Hilton York Hotel, York, UK

25 – 29 January 2010

This course is designed to teach the aspiring Qualified Person 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: £3105.00 plus VAT (First Booking)
£2484.00 plus VAT (Additional Bookings)

Cleaning Validation

Manchester Marriott Victoria & Albert Hotel,
Manchester, UK

2 – 3 February 2010

This ever-popular course will provide you with what you need to know to be able to design, execute and audit cleaning validation studies to current EU and US standards. There will be industry case studies on validation experiences for APIs, biotech products, solid dosage forms and medical devices.

Course Fee: £1320.00 plus VAT (First Booking)
£1056.00 plus VAT (Additional Bookings)

Formulation & Processing (Part 1)



Quality Leadership Program

Royal Sonesta Hotel, Boston, USA

2 – 4 February 2010

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 classes of pharmaceutical dosage forms.

Course Fee: \$2700.00
\$2160.00 (Early Bird and Additional Bookings)

Electronic Documentation and Annex 11

London Marriott Hotel Kensington, London, UK

2 February 2010

EU regulators have totally re-written their guidance on GMP requirements for computerised systems (Annex 11). Come and learn how the new Annex impacts on key areas such as electronic records and records retention.

Course Fee: £695.00 plus VAT (First Booking)
£556.00 plus VAT (Additional Bookings)



How to Simplify and Improve Your Computer System Validation



London Marriott Hotel Kensington, London, UK

3 – 4 February 2010

Computer Validation doesn't have to take an age, and consume vast amounts of resource! We will show you how to keep it simple and quick, whilst at the same time meeting EU and US requirements. **This course will save you money!**

Course Fee: £1320.00 plus VAT (First Booking)
£1056.00 plus VAT (Additional Bookings)

Risk-Based Decision Making in Sterile Products Manufacture

Manchester Marriott Victoria & Albert Hotel,
Manchester, UK

8 – 11 February 2010

How to use modern risk management techniques to take sound, science-based decisions on the types of incidents which can and do occur during the manufacture of sterile products. Essential education for Qualified Persons and technical staff.

Course Fee: £2275.00 plus VAT (First Booking)
£1820.00 plus VAT (Additional Bookings)

Book online at www.DBA-global.com

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

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GMP for Biological and Biotechnology Products

Manchester Marriott Victoria & Albert Hotel,
Manchester, UK

16 – 18 February 2010

This three day 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)

Human Error: Causes and Prevention

Manchester Marriott Victoria & Albert Hotel,
Manchester, UK

23 – 25 February 2010

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)

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

Manchester Marriott Victoria & Albert Hotel,
Manchester, UK

2 – 4 March 2010

The development of ICH Q8/Q8R (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)



Quality Management Systems

Qualified Person & Professional
Development Training



York Marriott Hotel, York, UK

8 – 12 March 2010

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: £3105.00 plus VAT (First Booking)
£2484.00 plus VAT (Additional Bookings)

Free Seminar for Prospective QP Trainees

York Marriott Hotel, York, UK

9 March 2010

Interested in becoming a Qualified Person? Why not attend this free seminar to find out more about what we can offer? Learn about what is required to become a QP and see one of our training modules in action.



Registering Drug Products in the EU: Quality (CMC) Requirements



Royal Sonesta Hotel, Boston, USA

16 – 18 March 2010

All you need to know about the practicalities of registering your drug products in Europe, including commonly made mistakes to avoid! Our European experts ensure no other US class comes close to this!

Course Fee: \$2675.00
\$2140.00 (Early Bird and Additional Bookings)



Get in touch now to book your place on any of these courses

Call us on: +44 (0) 1751 432 999 or email: courses@DBA-global.com

Forthcoming Courses

What's planned for the first four months of 2010



Practical Aspects of Pharmaceutical Validation

Manchester Marriott Victoria & Albert Hotel, Manchester, UK

22 – 25 March 2010

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)**

Risk-Based Decision Making

Marriott Philadelphia West, West Conshohocken, USA

23 – 25 March 2010

Unfortunately, things don't always go according to plan in our industry, and when they don't we have to take decisions about what to do next. Such decisions cannot be based upon emotion or "gut feel", but rather on the basis of facts, scientific understanding and a clear assessment of RISK. It is fair to say that regulators judge us by how we behave when things go wrong, not when they go right! We will provide you with tried and tested risk assessment and risk management techniques to ensure you make the right decisions at the right times! What is more, through a series of scenarios and case studies, we will demonstrate to you how your decision making skills have improved throughout the class.

**Course Fee: \$2675.00
\$2140.00 (Early Bird and Additional Bookings)**



Formulation & Processing (Part 2)

Quality Leadership Program

Royal Sonesta Hotel, Boston, USA

7 – 9 April 2010

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 classes of pharmaceutical dosage forms.

**Course Fee: \$2700.00
\$2160.00 (Early Bird and Additional Bookings)**



How to Simplify and Improve Your Deviation and CAPA System

Manchester Marriott Victoria & Albert Hotel, Manchester, UK

12 – 13 April 2010

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)**



Upgrading Your Quality Management System to Meet ICH Q10

Crowne Plaza Hotel Philadelphia – Downtown, USA

13 – 14 April 2010

ICHQ10, Pharmaceutical Quality System, is an industry-led initiative to provide much needed modern day guidance on the design, implementation and operation of a relevant and effective Quality Management System. Its adoption is having a profound affect on the way we work – now and in the future. Learn how best to apply this groundbreaking philosophy from someone who wrote it!

**Course Fee: \$1775.00
\$1420.00 (Early Bird and Additional Bookings)**



Book online at www.DBA-global.com

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How to Simplify and Improve Your Change Management System



Manchester Marriott Victoria & Albert Hotel,
Manchester, UK

14 – 15 April 2010

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)

How to Simplify and Improve Your Batch Record Review Process



Manchester Marriott Victoria & Albert Hotel,
Manchester, UK

19 – 20 April 2010

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)

KPIs and Performance Measures for Quality Systems



Manchester Marriott Victoria & Albert
Hotel, Manchester, UK

21 – 22 April 2010

This course will help you to set effective KPIs and performance measures for your Quality Management System and will teach you how to review them, interpret them 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)



Analytical Methods: Documentation, Validation and Transfer



Manchester Marriott Victoria & Albert Hotel,
Manchester, UK

27 April 2010

This new 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)

Investigating Out of Specification Results

Manchester Marriott Victoria & Albert Hotel,
Manchester, UK

28 April 2010

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)

Ongoing Stability Testing

Manchester Marriott Victoria & Albert Hotel,
Manchester, UK

29 April 2010

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)

Congratulations to:

In the past few months, DBA has helped the following people obtain QP status:

Colin Chambers, Renovo Ltd

Amanda Race, SSL International

Kathryn Rooney, Eli Lilly & Co Ltd

Get in touch now to book your place on any of these courses

Call us on: +44 (0) 1751 432 999 or email: courses@DBA-global.com

Industry News



PIC/S NEWS

Technical Interpretation of Revised Annex 1 to PIC/S GMP Guide Reinforces the Importance of 5 Micron Particles and Signals the End for Central, Manifold Particle Counting Systems

At the November 2009 meeting of the PIC/S Committee, it was agreed to adopt and publish a technical interpretation of key sections of the revised Annex 1, "Manufacture of Sterile Medicinal Products". This Annex is identical to Annex 1 of EudraLex Volume 4, commonly known as the EU GMP Guide. This, and the fact that EU regulatory agencies are members of PIC/S means that this interpretation will be applied by EU inspectorates at home and abroad.

The document, which was published and came into force on 1 December 2009, summarises the interpretations which an inspector from a national regulatory authority should adopt when performing an inspection of a manufacturer of sterile products.

Key Interpretations

- Grade A environments should be classified as ISO14644 class 4.8, not class 5. This is based upon the 5 micron particle limit of 20 (though why 20 was chosen instead of 29 is unclear).
- Central particle counters with long tube lengths will no longer be acceptable for clean room classification as they absorb too many particles – especially 5 micron particles. Similarly, the use of such particle counting systems for routine monitoring is discouraged.
- In critical areas with exposed product, continuous monitoring covering the duration of the operations is expected. Manifold

systems might not be suitable for Grade A zone monitoring due to a lack of responsiveness. It is also important that monitoring in Grade A covers equipment assembly.

- Continuous monitoring is expected in Grade B zones while "not fully integral" containers are handled (e.g. partially stoppered or uncapped vials). Again, manifold systems might not be suitable due to a lack in responsiveness.
- Any microorganism isolated from a Grade A zone should result in a thorough investigation. The organisms must be identified and impact on batch release should be considered.
- All microbiological sampling methods for which guidance figures are quoted in the Annex should be used for routine monitoring. If any methods are not used, a justification is required.
- If product sterilisation is achieved using two filters in series, bioburden samples must be taken immediately before the final filter unless the second filter is simply used as security in case one of the two filters fails, in which case the sample can be taken before the first filter in series.
- Where capping of vials is performed outside the aseptic filling room (so called "clean processing")...
 - ◆ Grade A conditions must be maintained up to the point of leaving the aseptic processing area and, thereafter, "Grade A air" should protect the vials until they are capped.

"Grade A air" is interpreted as meeting the requirements of Grade A only at "at rest" conditions, with the probe located underneath the filter. Smoke studies should be performed and, whilst unidirectional

air flow is not required, efficient protection of vials should be demonstrated. Limits for air velocity should be set and be justified. Additionally, particulate and microbiological monitoring is required in operation, with sites, frequencies and limits defined following a risk assessment.

- There should be a system capable of detecting displaced or missing stoppers prior to capping.
- The better the controls are for correctly set stoppers and demonstration of integrity, the fewer the requirements will be for the environment (e.g. Grade D rather than Grade C).

Thus, PIC/S continues to place heavy emphasis on 5 micron particles, even though there is no scientific evidence to suggest that such particles represent either a greater threat to product safety or a better assessment of the environmental cleanliness than 0.5 micron particles, even though ISO 14644 does not advocate classification of clean rooms by counting multiple particle sizes,

and even though FDA removed the need for enumeration of 5 micron particles many years ago.

Furthermore, this emphasis on 5 micron particles, coupled with the requirements to ensure that monitoring of Grade A and B zones is continuous, means that if you are still using a manifold-based particle counting system in your aseptic processing areas, PIC/S countries will require you to replace it with individual particle counters at each sampling location. This will undoubtedly add cost to the manufacture of sterile products – but will it add to product quality?

As for identification of every organism isolated from Grade A zones, the document doesn't state the extent to which identification should be taken; to genus, to species or even further. For guidance, see our article in Issue 5 of the DBA Journal (Spring 2007).

To download the entire PIC/S document, go to www.picscheme.org/news.php#n7

And just in case you are wondering which national regulatory agencies will be applying these interpretations, the 35 participating countries are...

Argentina	Finland	Latvia	Romania
Australia	France	Liechtenstein	Singapore
Austria	Germany	Lithuania	Slovak Republic
Belgium	Greece	Malaysia	South Africa
Canada	Hungary	Malta	Spain
Cyprus	Iceland	Netherlands	Sweden
Czech Republic	Ireland	Norway	Switzerland
Denmark	Israel	Poland	United Kingdom
Estonia	Italy	Portugal	

OTHER NEWS

China may Streamline Regulations for Device Registration and Trials

China's State Food and Drug Administration (SFDA) will soon no longer require device manufacturers to register products in the country of export as a condition of registration and will not

automatically require clinical trials in China for certain classes of devices. The changes are part of an overhaul of the country's device regulations in which the SFDA also says it will consider establishing an exemption from its requirement to test product samples in Chinese laboratories prior to approval if a device manufacturer demonstrates compliance with international standards and provides sound scientific evidence.

Industry News

EU NEWS

Medicinal Products

Revision of EudraLex Volume 4, Part 1, Chapter 7 (Contract Manufacture and Analysis)

In October 2009 the EMA published a Concept Paper stating their intention to revise this chapter to cover contracting out and “modern supply chain management”.

This is in response to global concerns regarding complex supply chains giving rise to risks of counterfeiting, adulteration and other serious quality problems.

EMA Reorganisation

In October 2009 the European Medicines Agency (EMA) announced that it had begun implementing a series of changes to its internal organisation aimed at improving the functioning of the Agency and the way in which it delivers its core tasks. The changes were to be introduced gradually from September to December 2009.

The resulting reorganisation includes the following key changes:

- The life-cycle management of medicines for human use is brought together into one Unit, Human Medicines Development and Evaluation, that will be responsible for the provision of advice during R&D, through to management of the review process and changes to products after they have been approved.
- The creation of a Unit, Patient Health Protection, contributing to patient health protection from the multiple perspectives of pharmacovigilance, risk and crisis management, patient and health care professional information, inspections (for both human and veterinary products), and appropriate regulatory compliance. The Unit will also be in charge of community procedures for both centrally and non-centrally authorised products.
- Within the Unit for Veterinary Medicines and Product Data Management:
 - ◆ the creation of a single Sector responsible for all areas of veterinary medicines – development, evaluation and maintenance of veterinary medicines, public and animal health (including safety) and veterinary regulatory affairs
 - ◆ the creation of a single Sector for the management of product data and documentation related to applications for the whole Agency; it will also be involved in the development of IT systems to support scientific business processes
- Rationalisation of services within the Unit for Information and Communications Technology.

UK NEWS

Medicinal Products

Herbal Products Trademark

In October 2009 the MHRA introduced a Traditional Herbal Registration (THR) certification mark, which is a type of trademark. This trade mark indicates that the herbal medicine has been registered with the MHRA under the Traditional Herbal Registration (THR) scheme. The THR mark is:



US NEWS

Recent Medical Device Guidance Documents

The FDA has recently published a number of guidance documents, including the following:

Guidance for Industry and FDA Staff – Implementation of Medical Device Establishment Registration and Device Listing Requirements Established by the Food and Drug Administration Amendments Act of 2007

Guidance for Industry and FDA Staff – User Fees and Refunds for Premarket Notification Systems (510(k)s)

Draft Guidance for Industry, User Facilities and FDA Staff: eMDR – Electronic Medical Device Reporting

Guidance for Industry, FDA Staff and Third Parties – Inspection by Accredited Persons Under The Medical Device User Fee and Modernization Act of 2002 and the FDA Amendments Act of 2007; Accreditation Criteria



Variations to UK National Marketing Authorisations

The new European Variations Regulation 1234/2008 comes into force on 1 January 2010. This new Regulation covers variations handled in Mutual Recognition or Centralised Procedures.

However, following a consultation earlier this year, UK health ministers agreed that the UK will adopt these new rules for all variations to marketing authorisations, including those held only in the UK. Therefore from 1 January 2010, the new classification systems and procedural rules will apply in full.

New UK guidance has been produced to assist those making variation

applications to the MHRA as from 1 January 2010, following the implementation of a new Commission Regulation and its adoption for UK national variations. This will be of particular interest to all active and trainee QPs in the UK.

Medical Devices

Borderlines with Medicines

The MHRA has published amended guidance on products on the borderline between medicines and medical devices. Historically, the UK's approach has not always been in line with that of other countries in the EU and recent changes have sought to minimise these differences. The major UK guidance

document, Bulletin 17, Medical Devices and Medicinal Products, was amended in August 2009 and includes a useful Annex which details, for different product types, whether medicines or medical devices regulations apply.

Borderlines with Other Products

Guidance Note 20, published August 2009, provides useful guidance on the borderline between medical devices and other non-medicine regulated products such as cosmetics, personal protective equipment, biocides and others. The document also provides examples of products which are, and products which are not medical devices.

ICH NEWS

ICH Q4B

The text of several Annexes to ICH Q4B, Pharmacopoeial Harmonisation, received either Step 2 or 4 approvals at the ICH meetings in 2009. These Annexes are:

- Annex 5, Disintegration Test, received Step 4 approval in June 2009
- Annex 7, Dissolution Test, received Step 4 approval in October 2009
- Annex 8, Sterility Test, received Step 4 approval in June 2009
- Annex 9, Tablet Friability, received Step 4 approval in October 2009
- Annex 10, Polyacrylamide gel electrophoresis (PAGE), received Step 4 approval in October 2009
- Annex 11: Capillary Electrophoresis and Annex 12: Analytical Sieving reached Step 2 approval in October 2009

ICH Q8(R2)

In August 2009 ICH Q8 (R2) was issued to reflect minor corrections to Example 2 on page 23; no other changes were made. The EU formally adopted this version in October 2009 and the USA adopted it in November 2009.

ICH Q8, 9 & 10 Implementation Working Group

A Q&A document was initially finalised (Step 4) in April 2009. In October 2009, a third set of Q&As was developed and approved by the ICH Steering Committee for integration in the Q&A document. This Q&A document is available from the ICH website www.ich.org

The IWG is also developing a training program for workshops that will be held in the three ICH regions that will cover the ICH Guidelines Q8, Q9 and Q10 with the aim of achieving globally consistent implementation. This training will consist of case studies representing the four phases of the life cycle of a pharmaceutical product. The workshops will be held in Europe in June 2010, in Washington DC in October 2010 and in Tokyo in November 2010.

Quality Leadership Program is launched to great acclaim



Our flagship education program for current and future pharmaceutical quality leaders and change agents, the Quality Leadership Program, was launched in Boston in October and the feedback from the first module (Pharmaceutical Law) was sensational!

Twenty four students from sixteen different companies across the US attended Module 1 and the vast majority have since signalled their intention to register for the Masters Degree that accompanies the program. Here are just some of the comments we received at the end of the module...

“It was very refreshing to come to a course with such content. Many times, classes just graze the top and only use buzz words. I look forward to the modules to come.”

“Fantastic course, great teachers, very good team exercises.”

“The tutors’ passion for the subject matter made the course!”

“Really loved the course and the presenters were extremely knowledgeable. Will recommend to others.”

At the time of writing this, we have a similarly sized audience for the second module in the program (Medicinal Chemistry) and initial feedback is equally positive!

Dates for future modules are as follows:

Module 3, Part 1	Formulation & Processing	February 2 – 4, 2010
Module 3, Part 2	Formulation & Processing	April 7 – 9, 2010
Module 4	Pharmaceutical Microbiology	June 2 – 4, 2010
Module 5	APIs/Supplier Assurance	August 3 – 5, 2010
Module 6	Mathematics & Statistics	October 13 – 15, 2010
Module 7	Analysis & Testing	December 7 – 9, 2010
Module 8	Pharmaceutical Packaging	February 1 – 3, 2011
Module 9	Quality Management Systems	April 4 – 6, 2011
Module 10	Practical	May 10 – 14, 2010
Module 11	Investigational Medicinal Products	August 2 – 4, 2011
Module 12	Role of the Quality Leader	October 3 – 5, 2011
All modules will be held at the Royal Sonesta Hotel, Boston, MA.		

If you would like to join the program but are concerned that you have missed the first two modules, don't worry. You can join or leave the program at any time. We aim to make this as flexible as possible to meet your needs!

For more information or to discuss how this program can benefit you...

Email: infoQL@DBA-global.com Call: 617-342-3625 Fax: 617-342-3623

DBA Analytical Partners with Virgo Publishing LLC to Offer Exclusive Industry Training Workshops at 2010 SupplySide East and West Conferences

DBA Analytical is now the exclusive provider of dietary supplement related trainings at the world's largest trade show and conference for healthy and innovative ingredients

Despite the global economic downturn, nearly 8,300 industry executives from global dietary supplement, food and beverage, and cosmeceutical companies participated in SupplySide West last November. Each year, more and more leading companies from across the globe convene to learn, network, and source at SupplySide East and SupplySide West. DBA Analytical is pleased to announce that we have signed an exclusive agreement with the creators of the SupplySide conferences, Virgo Publishing LLC, which means that these companies can also have access to the best cutting-edge quality and regulatory training for the dietary supplement industry.

In the last issue of the DBA Journal we discussed how training is the key to ensuring compliance to the increasing rigor of the US Food and Drug Administration (FDA) requirements and how DBA Analytical's training is both a cost-effective and efficient method of ensuring your company's compliance. The exclusive training agreement with Virgo Publishing will not only open up more opportunities for you to train your staff on important regulatory requirements, it will also result in time and cost savings by teaming with two industry-leading conferences.

DBA Analytical's training modules at the SupplySide conferences will focus on three areas – inspection readiness, standard operating procedure management (SOP) and corrective action and preventive action (CAPA) management.

Inspection Readiness

Inspection readiness training will provide attendees with useful background on the FDA and a complete breakdown of what to expect, and how to prepare for, a successful inspection. Other training components include:

- essential elements of a quality management system
- how to manage cross contamination
- risk and customer protection
- controlled temperature storage and distribution
- tips for a successful inspection

SOP Management

Standard operating procedures (SOP) are the cornerstone of a successful quality management system and help manufacturers integrate quality control mechanisms into their daily operations, helping to maintain safety and quality throughout the entire

manufacturing process. DBA Analytical's SOP management training covers every aspect of SOP development, including...

- the essential format and content requirements for SOPs
- who should write SOPs
- how to write effective SOPs
- the review and approval process for SOPs
- key requirements for controlled distribution of SOPs
- tracking, maintenance, change control and version control.

In addition, we will provide useful templates for attendees

CAPA Management

Another essential part of a quality management system is an effective corrective action and preventive action (CAPA) system. It is a regulatory requirement that the FDA, global regulatory inspectors and ISO auditors consider critical. When implemented properly, a CAPA system improves product quality and safety, increases customer satisfaction and, more importantly, verifies compliance with FDA and ISO requirements. DBA Analytical's CAPA management training equips trainees with all the knowledge they will need to start developing and implementing an effective and compliant CAPA system. Training components include...

- management, investigation and reporting of deviation incidents
- how to conduct and use a risk assessment
- the essential components of a deviation investigation
- how to prepare and follow through on corrective and preventive actions
- problem solving

The need to maintain and communicate quality has become a central theme to manufacturers and retailers of dietary supplements. Fortunately, DBA Analytical recognized this need for quality training and guidance nearly ten years ago by working collaboratively with their parent company, NSF International, and its Dietary Supplements Program, which offers GMP certification, as well as product and ingredients certification.

To learn more about DBA Analytical's exclusive training opportunities at upcoming SupplySide East and West conferences in 2010, contact Casey Coy for more details ccoy@dba-global.com.

Quality Management Best Practices

Managing Quality the 'Toyota Way'!

Background

Many pharma companies have now woken up to the fact that their Quality Systems are both ineffective and unaffordable. Not a pleasant situation to be in! For those of you searching for answers why not look outside the pharmaceutical industry? In fact if you're looking for industry 'best practice' for Quality Systems you need to look no further than Toyota.

'What can Toyota teach the Pharmaceutical industry?' I hear you say... well actually an awful lot! Toyota's philosophy and approach to quality management is generally regarded as world class, sustainable and **proven to work**. Crucially, their success is not down to a set of 'lean' tools or techniques, but an underpinning philosophy that focuses on only doing those activities that add value to internal and external customers. There is, however, a twist to the Toyota success story that serves as a painful reminder to all... more on this later.

But is it fair to draw comparisons between a manufacturer of cars and an industry making medicines? Although differences clearly exist, there are some striking similarities:

- Both industry sectors are heavily regulated. Although automobiles have no FDA or EMA equivalent, Toyota would argue that their activities are regulated by the most important and influential stakeholder of all...its customers. Like many other consumer industries, satisfy the customer and you stay in business. Upset them and you lose them for ever.
- The consumers of both demand high quality, affordable products.
- Both need to eliminate waste and non value adding activities to stay in business.
- Both have complex processes and products. The assembly of a 'Lexus' is probably more complicated than most pharmaceutical manufacturing processes.
- Both face the challenges of very complex supply chains.

So there you have it, manufacturing cars and medicines is actually quite similar! What is different is Toyota's approach to 'Quality Management.' For decades they have made cars more efficiently and with a lower defect rate than any other manufacturer. So how have they achieved this success?

The 'Toyota Production System'

Although the key principles of Toyota's Production System can be conveniently summarised it is vital to remember it represents a way of thinking, not just a set of tools and techniques. For those of you looking for a quick fix you may as well stop reading now. There isn't one. It's taken Toyota 60 years to create what they have and they still haven't finished!

So, what is the 'Toyota Way'? Their success has been achieved by:

1. **Adopting a Long Term Philosophy and Sense of Purpose:** Thinking beyond just making a profit.
2. **Investment in People:** 'We build people before we build cars'.
3. **Focusing on the Production Line:** 'Keep the main thing the main thing'.
4. **Being a 'Learning Organisation':** Continuously solving problems to learn.
5. **Focusing on the Process, not output:** 'The right process will generate the right results'.
6. **Standardising when ever possible.**
7. **The War on Waste:** The heart of the Toyota Production System.
8. **Supplier and Third Party Relationships:** The extended family.
9. **Performance Measurement:** Less IS more!



The 'Toyota Way'!

So, how does your company compare with the following?

1. Adopt a Long Term Philosophy: It's not just about making a profit

Until most recently, Toyota was different from most companies. Decisions are not driven entirely by satisfying short term profit and loss forecasts. They actually think beyond the desire to satisfy the accountants. Toyota plan and act with the long term in mind, not the quarterly results.

- They have strong commitment to serve and benefit society in general, not just shareholders.
- Toyota's mission and guiding principles is not a poster on the wall, they're practiced each and every day. They represent Toyota's 'moral compass' for routine and strategic decision making.
- Toyota has very little secrets. They even train their competitors in how to implement their 'Toyota Production System' so that other communities can benefit. They love to share best practice.
- The beliefs and values of Kiichiro Toyoda still drive the Toyota organisation. Successive leadership teams have worked hard to ensure these are passed onto the next generation. They work hard to protect and maintain the Toyota legacy.
- There is a constancy of purpose no matter how tough the environment. Their focus is to add value to customers, employees and society, not just shareholders.
- There is a very strong sense of purpose. 'Protect the legacy' even at the cost of short term profits. Day to day decisions are driven by the company's long term strategy. There is no short term thinking.

2. Investment in People: 'We build people before we build cars'

Every company says its products are only as good as its people. Toyota actually means it. They invest considerable effort in recruiting and keeping the very best. The recruitment of an assembly line worker can take up to 14 months before they are offered a full time contract. When asked:

"How can you afford this kind of recruitment process,"
Toyota's response is swift

"How can YOU afford not to?"

- Once they have recruited the best, people tend to stay. On average their staff turnover is less than 3%. Compare this with the 10-12%+ experienced by many pharmaceutical companies.
- They make a commitment to all of their employees 'Your job is



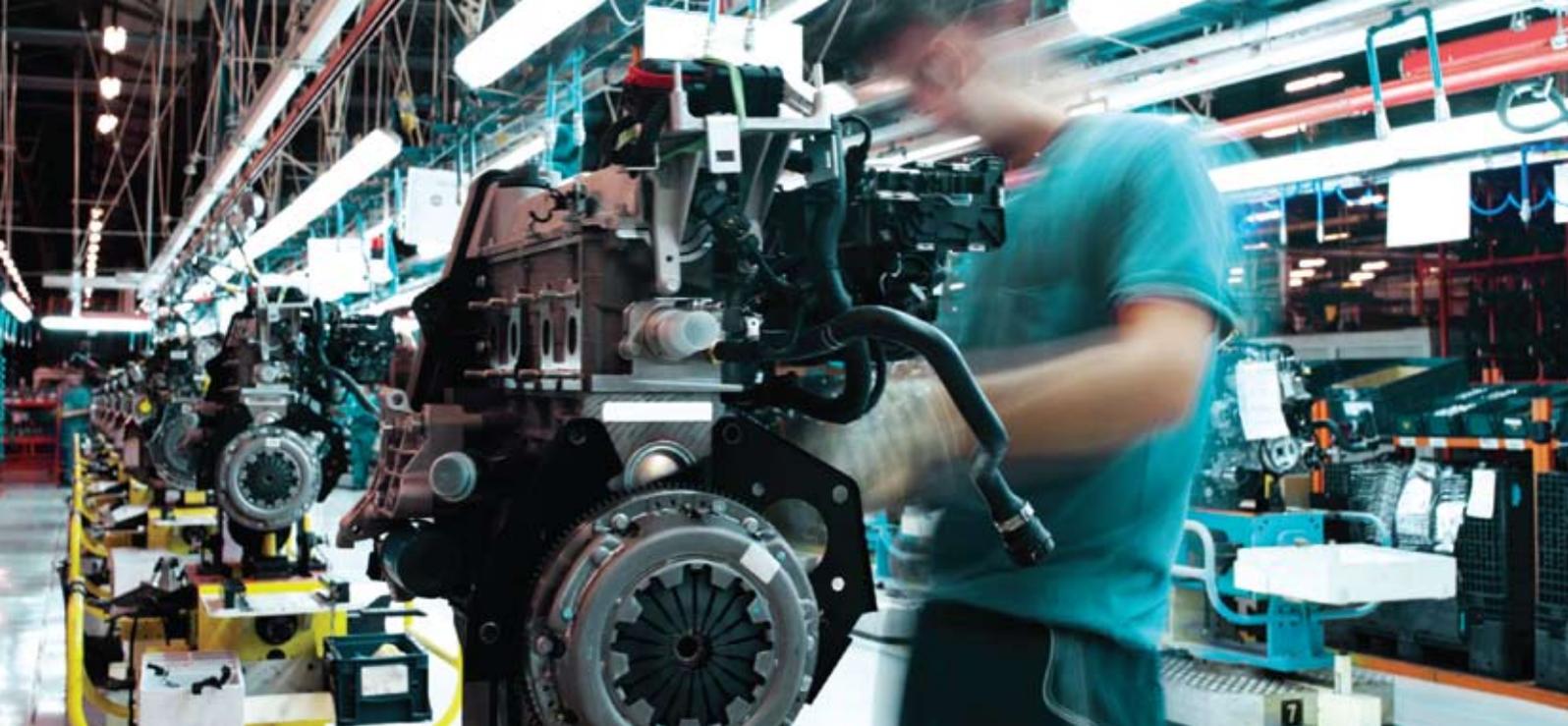
safe'. Even in the midst of the deepest financial crisis to hit the automobile industry in decades, Toyota has not made any full time employees redundant. Efficiencies and lean initiatives are used to create job opportunities, not make redundancies.

- Contractors and full timers are treated as equal in pay and privileges.
- Toyota reward team performance, not that of the individual. Promotion can take time. Slow promotion and rewards for team work is the norm.
- Toyota sees ongoing education as vital. They have even built their own University to ensure a steady flow of high quality engineers! They regard education as an investment, not a cost.
- Managers are seen as mentors and coaches, teachers not dictators.
- Toyota generally promote from within. They grow leaders rather than purchasing them.

3. Focus on the Production Line: Keep the main thing the main thing

Everyone focuses on servicing the production line. Every other activity is seen as 'non value added'. They achieve this by having:

- An 'upside down' management structure. Team leaders and managers support those at the sharp end, not the other way around. Assembly line operators are at the top of the pyramid, not the bottom.
- There is a genuine belief that only assembly operators and engineers add value. Everyone else must justify their reason for being!
- Everyone must serve their apprenticeship and develop deep understanding of the process. Even those in HR have 'time served' on the assembly line.
- Managers and team leaders spend up to 80% of their time on the production line solving problems and adding value – not in meetings or 'emailing'.
- Leaders manage from where the work is done, not from their office.



4. A Genuine Learning Organisation: 'Solving Problems is Key to Our Success'

- Toyota intentionally runs very, very lean. There are no buffer stocks to fall back on. Running lean means that problems can have a dramatic impact on production output. Problems **have** to be fixed, and fixed quickly.
- The pervading attitude is that problems and process deviations are **really** good news, providing you learn from them. It's accepted that 'real time' solving problems at source saves time and money later on downstream.
- Toyota famously adopts the 'andon' approach to problem solving. Deviations are acted upon within minutes and always solved at the site of the incident, never from behind a desk. Deviations are brought to the surface quickly and solved within hours. How does this compare with your '30 day' limit for deviations?
- Deviations are triaged (prioritised) and solved by teams of trained problem solvers, usually those at the sharp end using a standardised approach to problem solving and decision making. Recurrent problems are rare.
- Suggestion schemes are used to generate new ideas and ways of working with over 90% of suggestions implemented. Payments are weighted towards the small incremental improvements not the big ones.

5. ONLY Focus on the Manufacturing Process and nothing else

Toyota's attitude is 'get the process right and the results (output) will follow'. Most of their performance measures relate to the assembly process, not how many units are actually manufactured or rejected.

- They rarely use any new or unproven technology. They let

others suffer the cost and disruption of 'being the first'. Those at the sharp end are also involved in process design and the implementation of new technology. In fact they usually have the last say!

- Technology is only used when it can add value and keep things simple. Toyota's attitude is that people do the work, computers only move the information. If technology distracts or confuses the user, it is simply not used.

6. Standardisation is the name of the game

- Standardisation is considered as vital in order to stabilise any process. Just like the pharmaceutical industry, Toyota has SOPs to ensure processes are standardised to help guarantee a consistent output.
- Standardisation is about finding out the scientifically best way of doing a task, proving that it works and then 'freezing' it. Although people are expected to 'follow the rules' SOPs are not allowed to stifle innovation and further improvement. Users are encouraged to share best practice, 'hints and tips' and improve SOPs further. SOPs are constantly reviewed and improved, not every 2-3 years!
- The level of procedural compliance is very high for one simple reason – user involvement. SOPs are developed from the bottom up not from the top down. Management have very little input. Users are seen as the document owner. They write, design, refine and implement all new SOPs. Not surprisingly compliance is not a problem because they usually work!

7. The War on Waste: It never stops

Anything that adds no value is removed from the system.

- Toyota has created a continuous process flow for everything, removing non value adding activities from the system such as:

- ◆ Over production
 - ◆ Waiting
 - ◆ Unnecessary movement of anything, including people
 - ◆ Over processing
 - ◆ Excess inventory
 - ◆ Defects
 - ◆ Unused employee creativity
- Toyota also considers complex organisations and bureaucracy to be wasteful:
 - ◆ Rules and procedures are seen as ‘enabling’ and open to challenge, change and improvement. There is no such thing as ‘blind compliance’, following the rules for the sake of it
 - ◆ There is a ‘bottom up’ hierarchy. Corporate functions are small and very efficient

8. Supplier and Third Party Relationships

- Suppliers seen as an extended member of the family, an extension of the production line if you like.
- Toyota typically dual source most, but not all, components.
- Although Toyota depends heavily on suppliers they retain their core competencies to maintain self reliance and protect their intellectual property. They want to learn from suppliers but never transfer and lose core knowledge. Toyota wants to know what’s in the ‘black box’ and never lose internal capability.
- Toyota views any new supplier cautiously and starts with small orders first until trust and creditability have been established. This process can take up to 10 years for key suppliers.
- Toyota’s purchasing department includes quality experts who play a key role in the selection process. They never select on price alone and concentrate on building a long term ‘win:win’ relationship based on ‘fair and honourable business relationships’.
- Although they set very aggressive targets for service and quality, Toyota then provides the help and support needed to achieve these. Toyota actually helps suppliers improve their own business.

9. Performance Measures: Less is more!

- Less is more. Toyota measures only what is important and avoids the ‘death by measure’ approach adopted by many.
- They only select measures that drive the right behaviour. For example, assembly line workers are rewarded for raising deviations. After all, you learn more from your mistakes than from your successes. Contrast this approach with that taken by

many pharma companies, namely to encourage people to **reduce** deviation numbers! This measure drives completely the wrong behaviour.

The Twist to the Tale!

What Toyota has achieved can be replicated elsewhere; it **just** takes leadership and commitment! There is, however, a twist to this tale. For 50 years Toyota has led the market place with its performance, customer service and attitude to quality...until recently! In the last two years they have recorded annual losses. The company has also suffered embarrassing recalls in the USA. So what has gone wrong and, more importantly, what can we learn from Toyota’s recent experience? Independent observers put Toyota’s recent troubles down to:

- Senior managers focusing on the financial results and forgetting the basic principles that made the company great. Yes, the ‘financials’ are important but focus on them at your peril.
- The emergence of ‘lean fatigue’ and failing to keep focused on lean practices. The war on waste never stops.
- Failing to really fix problems with its customary patience and discipline, accepting compromises and ‘workarounds’ instead.

After years of success Toyota assumed that ‘quality’ was a given and something that could be achieved without paying attention to the ‘how’. The company’s top executives made the mistake of pursuing finance driven growth and pricing at the cost of sacrificing the principles that had made Toyota thrive. They took their eye off the ball.

For many pharmaceutical companies the facts remain unchanged. Quality Systems have to become more efficient and effective to stay in business. Although this transformation isn’t going to be easy, let’s learn from the best rather than reinvent the wheel.



Location, Location, Location

York: home to our Qualified Person & Professional Development training



We are proud to be a Yorkshire-based company, and even proud to host our flagship Qualified Person & Professional Development training courses in the wonderful old city of York.



One of the top tourist destinations in the United Kingdom, York combines history and culture with modern facilities and services to provide everything you need for a week's stay.



History

The city of York was founded as Eboracum by the Romans in 71 AD

and Roman walls and columns can still be seen around the city. Constantine was proclaimed emperor in York in 306 AD. The city was an important garrison for Roman troops venturing further north towards Scotland. The famous "lost" Ninth Legion set out on its fateful journey from York and some believe that ghosts of the legionnaires can be seen in the city.

After the Romans came the Vikings, who gave the city the name Jorvik, from which the modern name is derived. Jorvik was an important Viking city and remnants of the old city can still be seen at the Jorvik Centre in the city, where you can visit the site of Viking Jorvik and experience what the settlement was like.

Although the Viking city is now long gone, many buildings from medieval York still remain. The "Jewel in the Crown" is York

Minster – the largest gothic cathedral north of the Alps and one of the finest medieval buildings anywhere on the planet. Visitors to York should ensure they visit the Minster at least once; it is an unforgettable experience.

The Minster is surrounded by medieval streets dating back 500 years and more. Perhaps the most famous (and most photographed) is The Shambles, where butchers used to ply their trade. At the end of The Shambles is the shortest street in the city with the longest name: Whippawhopmagate. Because of its long history, York is considered to be one of the most haunted cities in the world. Every day you can join one of many Ghost Tours of the city – best taken after dark!

Culture

York has two world class museums, the Castle Museum (which includes a reconstructed Victorian shopping street) and the National Railway Museum (which pays homage to Britain's role in bringing railways to the world and houses engines from all ages and countries). Both museums are a "must".

York is also home to two fine theatres and a number of music venues catering for all tastes, from early music to the latest pop and rock.

Modern York

Although firmly rooted in history, York is a modern, vibrant city. Its shopping areas, hotels and restaurants are some of the best in Northern England.

Our two hotels, The York Hilton in the city centre and the Marriott Hotel by the racecourse, provide all the services that a modern business traveller needs, with the unique added bonus of easy access to some of the finest historical buildings anywhere in Europe.

No wonder we are proud to invite our clients to join us in the magnificent city of York. Why not pay York – and us – a visit? We promise you won't be disappointed!

To learn more about what York has to offer, visit www.visityork.org/

In the next DBA Journal: Industry News: As ever we search for regulatory changes so you don't have to; Tech Talk: How to benchmark your Quality Management System against the best; DBA People: Helping you to get to know us better; Forthcoming Courses: A review of our education programmes for late Spring and Summer; 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@DBA-global.com

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