DBA

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The Journal of David Begg Associates

Issue 3 Summer 2006

Course Updates

What David Begg Associates courses are coming up in the late summer and autumn.

Industry News

The latest pharmaceutical industry news with Bob Pietrowski.

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David Begg associates

David Begg associates

welcome

Summer is almost here!

Days are getting longer and warmer, the sun is high in the sky. Summer is almost here and we are half way through 2006!

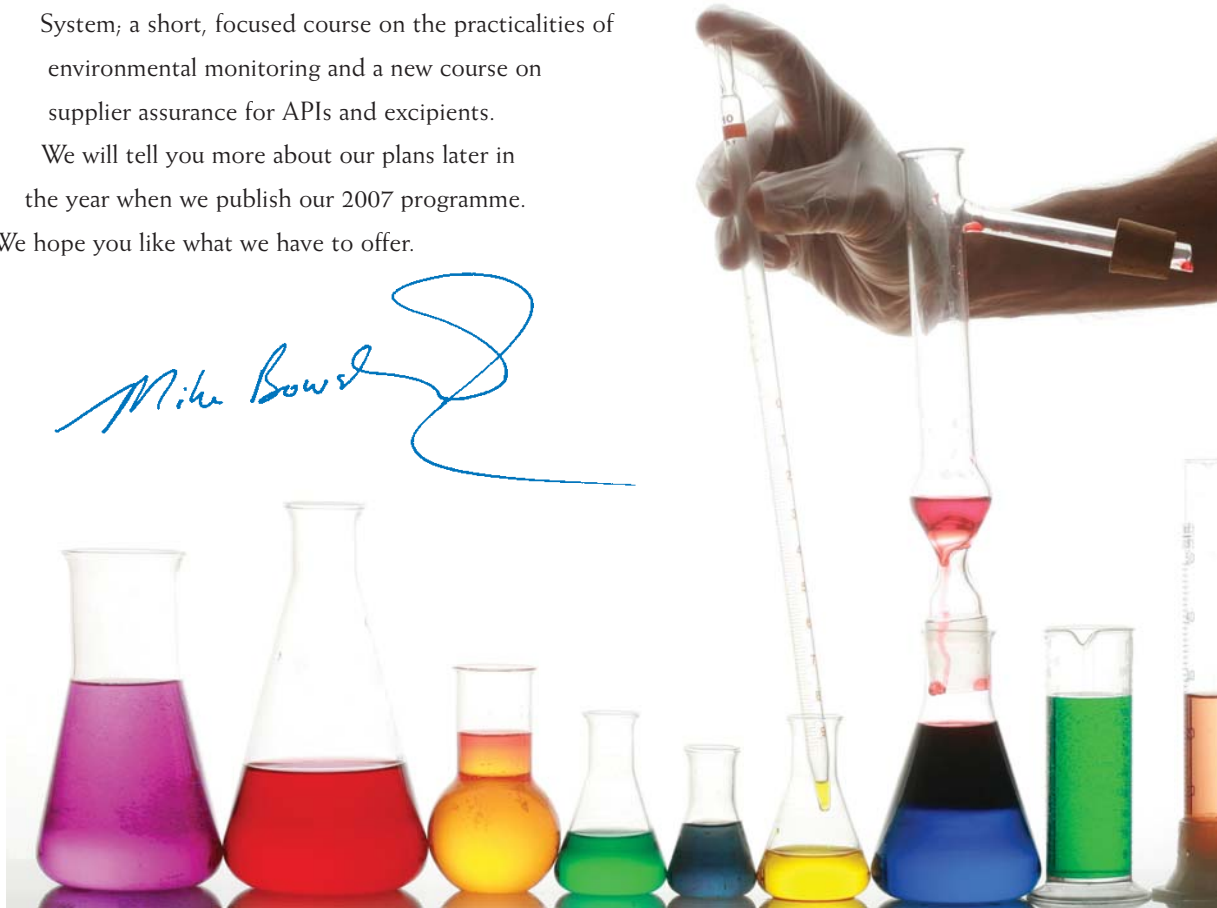
The first half of this year has been very successful for everyone here at DBA – attendances at our training courses have been the best ever (thank you all!) and our consultancy and auditing services have been so popular that we are recruiting more staff to meet demand. Like you, we need a summer holiday to recover and re-charge our batteries!

Mike Bowsher,
Managing Partner
David Begg
Associates

Looking Ahead to 2007

While you have been planning your summer vacations, we have been planning our 2007 training programme. We have retained all the "old favourites" and have added a few new topics which we hope you will enjoy. These include a course on designing an effective Quality Management System; a short, focused course on the practicalities of environmental monitoring and a new course on supplier assurance for APIs and excipients. We will tell you more about our plans later in the year when we publish our 2007 programme. We hope you like what we have to offer.

Mike Bowsher



Industry News

EU Publishes Proposed Revision of Annex 7 "Manufacture of Herbal Medicinal Products"

The European Union has published a draft revision of Annex 7 for industry comment. The draft contains significantly more guidance and has been prompted by adoption of Directive 2004/24/EC on traditional herbal medicinal products.

The main changes are…

Emphasis is placed on the importance of seed selection, cultivation and harvesting in assuring the quality of the herbal medicinal product. The Annex now references recommendations on "Good Agricultural and Collection Practice," first published by EMEA in 2005.

A very helpful table is included in the opening section of the Annex which identifies those activities to be conducted in accordance with Good Agricultural and Collection Practice, those to be conducted in accordance with Part II of the EU GMP Guide (such as cutting, drying, extraction and purification of the herbal substance) and those to be conducted in accordance with Part I of the EU GMP Guide (processing into a dosage form and packing)

Emphasis is placed on procedures to detect adulteration of the herbal substance and on security sieving to remove foreign matter prior to processing

A reference sample of the plant material is required to be held by the manufacturer.

Industry has until 31 July 2006 to comment on the draft.

Issues surrounding the licensing, manufacture and control of herbal medicines and many other medicinal products will be discussed in detail in Module 1 of our new series of Qualified Person and Professional Development training. The module, "Law and Administration" will be held at the Marriott Hotel, York from 9 to 13 October 2006.

ICH Starts Work on Q10: GMP Quality Systems

Following on from the success of ICH guidelines Q8 "Pharmaceutical Development" and Q9 "Quality Risk Management", ICH have started work on the long discussed and eagerly awaited guideline Q10 "GMP Quality Systems".

Work to produce Q10 started in Chicago in November 2005. The aim is to create a bridge between existing US, EU and Japanese GMPs. Initial discussions have agreed that the guideline should create essential elements of a broad, comprehensive quality system which covers the whole product life cycle for both medicinal products and APIs. Thus the guidelines will include process development, routine manufacture and the difficult and often ignored topic of technology transfer.

Those developing the guideline aim to draw heavily on existing documents such as the ISO 9000 series of documents on Quality Management Systems, ICH Q7 (GMP for APIs) Eudralex Volume 4 (the EU GMP Guide), FDA's draft guidance from 2004 on a Quality System approach to cGMP and ISO 13485, Quality Management Systems for Medical Devices.

Given the scope of ICH Q10, it is a pity that work on this guideline could not have run in parallel with that for Q8 and Q9.

However, it is to be hoped that, when complete, Q10 will complement these two guidelines and take us closer to gaining international consensus on what constitutes appropriate quality management and GMP.

It is anticipated the draft guideline will reach Step 2 of the ICH process by spring 2007.

This and other topics will be covered in detail in our new course "Designing and Operating an Effective Quality Management Systems" to be held in Manchester from 5 to 8 March 2007. More details will be published on our website shortly.

Forthcoming Courses

What's planned for the next six months, July to December 2006

Microbiological Risk Assessment

Hilton Hotel, Cobham, UK

4 – 6 July 2006

Designed for both microbiologists and non-microbiologists, this three day course is designed to teach you how to use risk assessment techniques such as FMEA and HACCP to identify the critical control points in your processes, how to apply control measures and how to assess the risk associated with incidents and failures, so you can really bring your processes under effective control.

Course Fee £1,490.00 Plus VAT

Compliance Issues for Computerised Systems

NEW course

Marriott Victoria & Albert Hotel, Manchester, UK

4 – 6 July 2006

Brought forward and extended by popular demand! This three day course will teach you all you need to know about EU and US regulatory expectations for computerised systems and will provide you with practical advice on how to satisfy these requirements efficiently and cost-effectively. Taught by two of Europe's leading experts in the field.

Course Fee £1,490.00 Plus VAT

Pharmaceutical Good Manufacturing Practice

Hilton Hotel, Cobham, UK

18 – 21 September 2006

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

Course Fee £1,945.00 Plus VAT

Good Documentation Practices

Manchester Airport Marriott Hotel, UK

19 – 20 September 2006

This course is essential for anyone wishing to make their documentation system more efficient, cost-effective, user friendly and compliant with EU and US GMP requirements. The course will be highly participative – you will design key documents and perfect your document writing skills.

Course Fee £1,130.00 Plus VAT

Book online at www.david-begg-associates.com

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GMP for Clinical Trials Manufacture and Supply

Hilton Hotel, Cobham, UK

2 – 5 October 2006

Essential training in current EU and US GMP regulations for the manufacture, testing, importation and distribution of clinical supplies. Keynote talk by a European regulatory inspector.

Course Fee £1,945.00 Plus VAT

Pharmaceutical Law and Administration
Qualified Person & Professional Development Training

Marriott Hotel, York, UK

9 – 13 October 2006

All the prospective Qualified Person or pharmaceutical professional needs to know about EU, UK and US pharmaceutical legislation and regulatory bodies. This course provides the depth of knowledge and understanding you really need to act in a professional capacity in a highly regulated industry.

Course Fee £2,800.00 Plus VAT

Free Seminar for Prospective Qualified Persons

Marriott Hotel, York, UK

10 October 2006

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

Pharmaceutical Legislation Update

Manchester Airport Marriott Hotel, UK

17 October 2006

Continuing professional development for Qualified Persons and other technical personnel. You will learn about current and proposed changes to legislation and GMP requirements in EU and USA and their impact on QPs and technical managers. Your annual top up!

Course Fee £595.00 Plus VAT

Pharmaceutical Packaging GMP – Compliance at the Operational Level

Marriott Victoria & Albert Hotel, Manchester, UK

31 October – 2 November 2006

Key EU and US GMP requirements for pharmaceutical packing operations, including up to the minute developments in security systems and ISO GMP expectations for primary packaging components.

Course Fee £1,490.00 Plus VAT

Forthcoming Courses (cont)

What's planned for the next six months, July to December 2006

Good Autoclave Practice

Clontarf Castle Hotel, Dublin, Ireland

7 – 9 November 2006

A comprehensive course on the practicalities of autoclave selection, equipment qualification, cycle design and validation, ongoing performance monitoring and management. You will learn current regulatory expectations for steam sterilisation, how to qualify and validate autoclaves effectively, how to troubleshoot problems and best industry practices for monitoring and management of autoclaves.

Course Fee £1,715.00 Plus VAT

Chemistry and Pharmacy Registration Requirements

Hilton Hotel, York, UK

13 – 16 November 2006

Run in conjunction with Regulatory Resources Group, this course is designed to provide you with a clear understanding of technical data requirements for EU and US registration submissions and subsequent manufacture.

Course Fee £1,945.00 Plus VAT

Medicinal Chemistry and Therapeutics
Qualified Person & Professional Development Training

Hilton Hotel, York, UK

20 – 24 November 2006

All the prospective Qualified Person or pharmaceutical professional needs to know about how drugs act on the body, the major therapeutic classes of drugs and how these drugs should be handled in manufacturing.

Course Fee £2,800.00 Plus VAT

A-Z of Pharmaceutical Water Systems

Marriott Victoria & Albert Hotel, Manchester, UK

27 – 30 November 2006

This four day course will provide you with up to date information on EU and US regulatory expectations for water systems and practical advice on system design, validation, monitoring and management as well as trouble shooting and risk assessment. In short, all you will ever need to know about water systems!

Course Fee £1,945.00 Plus VAT

DAVID BEGG ASSOCIATES 20 YEARS PROFESSIONAL EXCELLENCE 1986-2006

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

Call us on +44 (0) 1751 432999

email: courses@david-begg-associates.com

Tech Talk

Issues Affecting The Qualified Person

In this Journal, we concentrate on issues impacting the Qualified Person and those training to become Qualified Persons.

QP Discretion and Batch Release

The legal duties of the QP are laid down in Directives 2001/82/EC and 2001/83/EC. Amongst these is the requirement to ensure that each batch of medicinal product has been manufactured in accordance with the requirements of the Marketing Authorisation. However, we all know that, from time to time, deviations to manufacturing processes occur. Some of these have significant implications for the quality and safety of the batch, which must not be released. Others, however, have no patient safety implications. Can these batches therefore be certified and released by the QP even though they are not in compliance with the Marketing Authorisation?

This thorny issue first came to prominence in the UK in December 2000 when the regulatory authority published a document stating that the QP did not have the legal discretion to certify and release batches that did not comply with the Marketing Authorisation. This theme was picked up by the Irish Medicines Board, which published a very similar statement.

we all know that, from time to time, deviations to manufacturing processes occur

In January 2004, EMEA published a document (EMEA/INS/GMP/47/04) which essentially echoed the UK and Irish sentiments on QP discretion. The document caused something of a stir in European industry circles and was subsequently withdrawn.

It is clear that there is no harmonised approach to QP discretion and batch release within the EU. This represents a problem to the regulators and also to the manufacturers, who must operate on an international basis. As a result, EMEA asked the Irish Medicines Board to prepare a set of proposals on the issue for internal discussion. These have ultimately led to EMEA publishing in March of this year a "Reflection Paper" on a proposed solution for dealing with minor deviations from the detail described in the Marketing Authorisation. The reflection paper contains only proposals, is not legally binding, and is published to invite comment.

The paper emphasises that:

Any deviation/non–compliance, which may materially affect the safety of efficacy of a batch of product, or compromises the overall product quality, must result in a QP decision not to release that batch.

Recurrent deviations from the manufacturing process and/or analytical control methods as approved in the Marketing Authorisation application dossier, even though judged minor, are changes and variations to the affected Marketing Authorisations are necessary.

Given these and other provisos, this paper proposes that a batch of finished product can be considered to continue to meet the requirements of the Marketing Authorisation when:

1. **The deviation is minor, one-off and unplanned in nature and relates only to the manufacturing process and/or the analytical control methods of either the starting materials or the medicinal product as described in the Marketing Authorisation.**
2. **The active substance/antigen and finished product specifications are complied with.**
3. **An assessment is performed by the manufacturer using the approaches described in ICH Q9, Quality Risk Management, to support a conclusion that the occurrence is a minor quality deviation that does not affect the safety and efficacy of the product.**

The risk assessment should assess the need for inclusion of the affected batches in the ongoing stability programme as required by Chapter 1 of the GMP Guide and the whole process should be integrated into the manufacturer's quality assurance system, notably the documentation system established to comply with GMP, and record be available for inspection by the Competent Authorities.

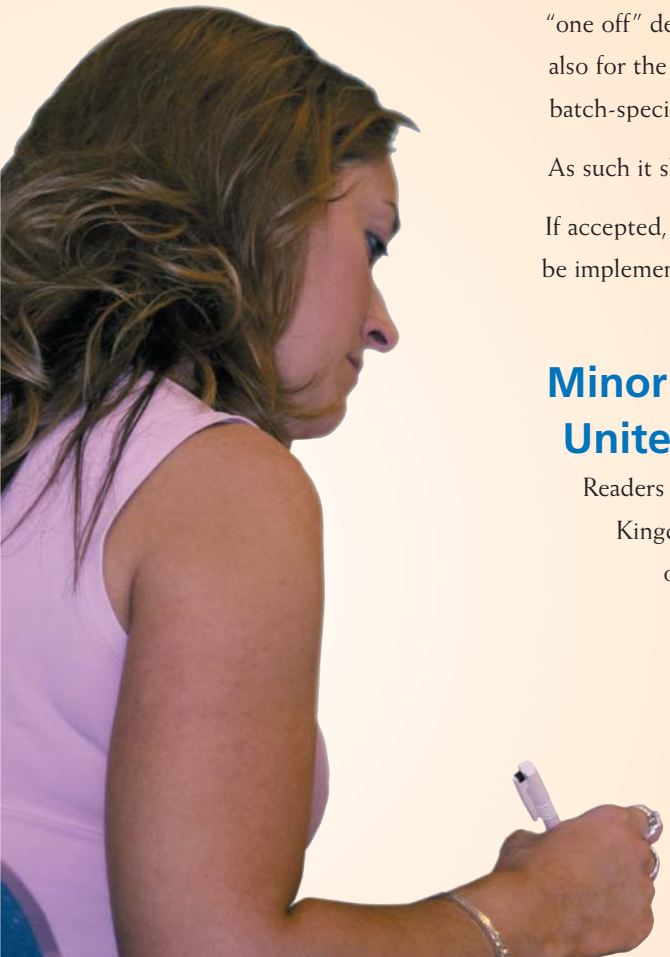
All such deviations must be reviewed as part of the annual product quality review as required by Chapter 1 of the GMP Guide.

Trends or recurrences and other deviations from the details of the Marketing Authorisation must be flagged as problems that require resolution with the Competent Authorities including, if necessary, the submission of variations. The proposed solution described above does not apply in these circumstances.

The Reflection Paper re-emphasises the basic principle that the QP may not certify or release a batch of medicinal product which fails to comply with the Marketing Authorisation without recourse to a variation, but enforces this principle for recurrent rather than "one off" deviations. This represents a pragmatic solution for the manufacturer and also for the regulators, as there is currently no EU-wide mechanism for approving batch-specific variations.

As such it should be welcomed by Qualified Persons.

If accepted, it is proposed that the principles of this reflection paper will eventually be implemented as an amendment to Annex 16 of the GMP Guide.



Minor Revisions to the United Kingdom Study Guide

Readers are probably aware that prospective Qualified Persons in the United Kingdom must undergo an "interview" with representatives of the Institute of Biology, the Royal Society of Chemistry and the Royal Pharmaceutical Society of Great Britain. During this interview, the candidate is questioned on topics relating to pharmaceutical law, the duties of the Qualified Person and the essential elements of Quality Management (the three 'foundation knowledge' areas), as well as a range of topics pertinent to the manufacture and control of

medicinal products. The "body of knowledge" expected of the candidate is broad and is defined in a Study Guide, which is published by the three professional bodies mentioned earlier following consultation with the regulatory authorities.

The professional bodies have revised the Study Guide in recent months and the new version came into effect on 1st May 2006.

The majority of the changes to the Study Guide reflect the changes in European pharmaceutical legislation since the last Study Guide was published in 2000. There is thus increased emphasis on the role of the Qualified Person with respect to investigational medicinal products and clinical trials, active pharmaceutical ingredients, traditional herbal medicines and topics such as product quality reviews. Similarly, there is now mention of ICH Q9, Quality Risk Management, in the section on Quality Management Systems.

the major change comes in the specific knowledge expectation

Perhaps the major change comes in the specific knowledge expectations for candidates and their ability to apply that knowledge. The Study Guide now states…

"The three professional bodies require an applicant for certification as a Qualified Person to demonstrate foundation knowledge and to be able to apply his or her knowledge of QMS principles, and will also be expected to demonstrate understanding of the additional knowledge requirements. The applicant will be required to demonstrate this by reference to the products and processes for which he or she is claiming his or her qualifying experience."

Thus, candidates can expect to be asked questions which test their practical understanding of pharmaceutical manufacture and control, rather than just the theory, and which concentrate on those products and processes which are familiar to the candidate.

A new application form has been prepared to compliment the Study Guide and this should be used for all applications from now on, although the professional bodies will still accept applications on the old form.

The professional bodies will be happy to answer any queries from prospective QPs.

Our Ninth Series of Qualified Person and Professional Development Training Modules starts in October.

David Begg Associates, in conjunction with the University of Strathclyde, have been offering training to prospective Qualified Persons since 1990. Our ninth series of modules begins with "Pharmaceutical Law and Administration" at the Marriott Hotel York from 5th to 8th October 2006.

If you would like to join us or would like further information about the training we offer, please contact Stella Pearson-Smith on +44 (0) 1751 432999 or email her at qp@david-begg-associates.com.

Location, Location, Location...

Introducing the Marriott Manchester Victoria & Albert Hotel, one of Manchester's premier hotels.

Located in a converted Victorian warehouse, this lavishly appointed hotel combines the convenience of a city centre location and high quality accommodation with easy access to a major international airport.

We introduced the Marriott Manchester Victoria & Albert Hotel into our range of venues late last year in response to your request for more convenient locations. From day one, the hotel has been a huge success, winning rave reviews from our delegates.

This is not surprising, since the hotel offers very high standards of accommodation at reasonable cost, as well as easy access to Manchester city centre and swift links with Manchester International Airport (less than 30 minutes away by taxi or train).

Formerly a Victorian warehouse on the banks of the River Irwell, the hotel has been modernised at great expense, but it retains the period flavour – wooden ceilings are supported by oak beams and cast iron pillars in all rooms.

Manchester city centre is only five minutes walk from the hotel and offers a wealth of shopping opportunities and a huge variety of restaurants.

Should you wish to extend your stay to take in some sightseeing, the city has numerous excellent theatres, museums and art galleries, including the world famous Lowry Centre, whilst the sport-minded can tour Old Trafford, the home of Manchester United FC, and perhaps even attend a midweek match.

Shopaholics can visit the nearby Trafford Centre – one of the largest shopping malls in Europe.

We love the Marriott Victoria & Albert Hotel and we are sure you will too! We shall be hosting the following courses at the Victoria & Albert Hotel in the second half of 2006:

- Compliance Issues for Computerised Systems
  4 – 6 July 2006
- Pharmaceutical Packaging GMP
  31 October – 2 November 2006
- A – Z Pharmaceutical Water Systems
  27 – 30 November 2006.

DBA People

Fuji Photography!

In each Journal we spotlight a member of the DBA team so that you can get to know us better. In this issue it's Peter Gough.

Peter Gough joined us just over a year ago and it soon became apparent that he is a man of passion!

Well, three passions in fact…

Pharmaceutical Quality risk Management – Pete played a huge part in writing ICHQ9

Rock music – Pete has the fullest and most varied iPod of all of us!

Photography – Pete is inseparable from his camera – he takes it wherever he goes and makes the most of his business trips to capture images and landscapes which serve not only as mementos, but also a as pieces of art which adorn the walls of his office (along with works by Pete's wife Sue, who is a painter and printmaker). As well as being a hobby, photography provides an opportunity for quiet contemplation after a hectic day of training or consultancy.

One of Pete's favourite work-related photographs is shown here – a rare glimpse of Mount Fuji captured from his Yokohama hotel bedroom during one of the ICHQ9 meetings.

For the geeks amongst you, Pete uses a Nikon 8800, 8 mega pixel digital camera with a 35 – 350 mm equivalent zoom. For the rest of you, it's big and black!

Congratulations to:

in the past four months, DBA has helped the following people obtain QP status:

Leonor Arrebola, Ceutocor BV, Netherlands, **Nick Brand**, AstraZeneca, UK, **Emily Rumsey**, Baxter Healthcare Ltd, UK, **Mark Sephton**, Napp Pharmaceuticals Ltd, UK, **Jennifer Watson**, SSL International, UK.

In the next DBA Journal.

Industry News as ever, we search for regulatory changes so you don't have to, Tech Talk a beginner's guide to risk assessment techniques, Location, Location, Location…The Clontarf Castle Hotel, Dublin, DBA People Peter Smith's "TV Star" car, Forthcoming Courses a review of training courses for Winter and Spring 2007.

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

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