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NSF DBA℠

Supply Chain

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welcome

Bob Pietrowski
Managing Partner
NSF-DBA

Welcome to the latest edition of the NSF-DBA Journal. You will see that this Journal has a strong focus on one of the most important issues facing the health science industry today – ensuring the integrity of the supply chain.

The health and wellbeing of patients worldwide is currently being threatened by two serious (potentially deadly) criminal activities: the deliberate adulteration of active ingredients and starting materials and the illegal manufacture and supply of counterfeit healthcare products, both for financial gain and with absolutely no regard for human safety. The fight against these illegal activities requires the active participation of organizations at many different levels and in many different countries. Foremost in this struggle will be the regulatory agencies and, of course, the reputable manufacturers.

In this issue, Pete Gough describes how regulators in the European Union have responded to the threat of adulterated starting materials and the huge challenges that recent and impending regulations pose for manufacturers of healthcare products.

Elsewhere in this issue we challenge businesses on their QMS systems and ask "Are they fit for purpose?", while Neil Wilkinson introduces our expanding team in the Boston office. We include all the usual features, the latest Industry News and our training courses for the first months of 2013.

We hope you enjoy this latest edition of the Journal.

Bob Pietrowski
Managing Partner

NSF DBA The Health Sciences, Training, Consultancy and Auditing Experts SM

Tech Talk

Supply Chain Assurance

As the European Union tries to get a grip with counterfeit medicinal products through legislation, Pete Gough discusses the headache globalization of pharmaceutical API manufacture is causing to the industry.

The discovery of contaminated Heparin in 2008 focused global attention on the need for greater security of pharmaceutical supply chains. Preceding this there had been a worrying increase in the number of counterfeit medicinal products reaching legitimate supply chains but it was the Heparin incident that really brought the issues into sharp focus. Since 2008 various events have only confirmed that there are real risks to patients from deliberate adulteration and counterfeiting of medicines or their ingredients; eg melamine in milk, chromium in gelatine, plasticisers in antibiotics, fake Avastin, to name but a few. It has been estimated that globally around 10% of medicinal products are counterfeit, however, the proportions are still much lower in the developed world but can be as high as 80% in parts of the third world.

In July 2011 the EU published Directive 2011/62/EU, the Falsified Medicines Directive (FMD) and in June 2012 the US Congress passed the FDA Safety and Innovation Act (FDASIA). Both of these far reaching pieces of legislation seek to impose much stronger controls on pharmaceutical supply chains and the implications for the manufacturers of medicinal products and their suppliers are very significant.

Looking at the FMD first, many of its provisions are sensible, proportionate and should provide increased safety for patients:

- Active Pharmaceutical Ingredient (API) supply to comply with Good Distribution Practice (GDP) as well as being made to GMP
- Excipients to be made to an appropriate level of GMP determined by a formal risk assessment
- The legal obligation for the users of APIs and excipients to map and audit their supply chains for GMP and GDP compliance
- The need for "importers, manufacturers and distributors of active substances" in the EU to register with the Competent Authority of the Member State where they operate and be required to submit at least annual reports of changes to the Authority
- The addition of "Safety Features" to packs of medicinal products

Unfortunately, the FMD also contains a requirement that has the potential to seriously reduce the availability of medicinal products in Europe and to drive even more medicinal product manufacturing out of the EU/EEA. This is the poorly thought through requirement that, from July 2, 2013, APIs shall only be imported if the active substances are accompanied by a written confirmation from the Competent Authority of the exporting third country, and the plant manufacturing the exported active substance confirms that the standards of GMP and control of the plant are equivalent to those in the EU.

Tech talk

By early November 2012 just five countries had applied to the Commission to be added to the list of countries exempt from the need for this certification; Switzerland, Israel, Australia, Singapore and Brazil. None of these had been approved at that time. Many countries have responded negatively to the requirements from Europe seeking to impose this extra-territorial obligation on them. Even the EU's ICH partners, the USA and Japan, have yet to decide if they will be prepared to issue the required API certificates.

India and China are, reportedly, considering jointly referring this to the World Trade Organization (WTO) as it constitutes a technical barrier to trade. S Eshwar Reddy, India's Deputy Drug Controller, was recently reported in the online newsletter in-Pharma Technologist.com as having stated that "If the importing country has specific GMP requirements, that is their responsibility to audit the facilities. It is the responsibility of the importing country, not the exporting country."

India is a major supplier of APIs to the EU and whilst it has indicated that it will set up an Authority to issue the required certificates it will do so on the basis of just a half-day visit to each API site, which while complying with the letter of the new requirement offers no real additional supply chain assurance.

This potentially means that after July 2, 2013 if a medicinal product manufacturer is unable to obtain the required certification for the API imported into the EU they will have to cease production of their product. This will potentially lead to the shortage of some medicines across the EU, which perversely may encourage counterfeiting to fill the gaps. It is possible that in their naivety the European Commission introduced this requirement in an attempt to drive more API manufacture within the EU. However, it is far too late for this as over the past 15 or so years much of the EU's infrastructure to manufacture APIs has closed and there is little prospect of significant re-investment in this area in the currently depressed economic climate. The more likely consequence is that companies will choose to also move their secondary manufacturing outside of the EU as the importation of fully finished medicinal products avoids the need for the certification of the API. This requirement can only do further damage to the pharmaceutical industry in Europe, which was once such a powerhouse of the European economy, but is now shrinking rapidly under an ever increasing burden of poorly thought through legislation coming from Brussels.

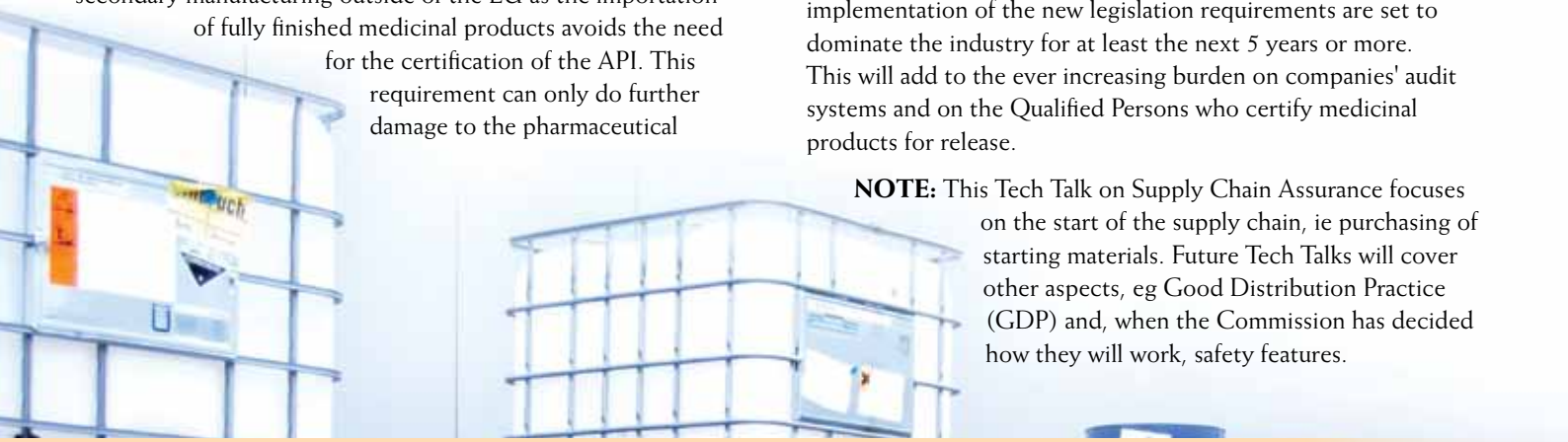
Most of the provisions of the FMD are sensible precautions to protect EU citizens from counterfeit products. It is a shame that the European Commission chose to try to impose their certification scheme for APIs on the rest of the world; it would have been far better to foster co-operation with foreign governments to try to defeat this immoral trade. The current certification requirement will almost certainly be ineffective and counterproductive, antagonizing and annoying the rest of the world and driving even more medicinal product manufacturing overseas while providing little or no extra supply chain assurance.

The US FDASIA appears to be a better thought through piece of legislation, although there is still a lot of detail to be clarified in new rules and guidance from FDA. For a review of the FDASIA see the 'News' section on page 6 of this issue of the Journal.

One feature of both the European FMD and the US FDASIA is the introduction of a system to verify the authenticity of a medicinal product at the point of dispensing, what the EU has called "Safety Features" and the Americans call "Track and Trace". Both regions are working on this and it would certainly be helpful to the manufacturers of finished product if the requirements were, if not identical, at least similar. The implementation costs of these systems are going to have to be largely borne by the pharmaceutical industry. The industry literally could not afford to equip its packaging facilities to accommodate totally different systems in the US and EU. There have been good links forged between the EMA and the FDA over the past 10 years or so; hopefully, they will not develop totally different systems. Most people in the EU are expecting the system for adding the serialization number to packs to be based on a 2D bar code as the most practical and economic option.

Concerns over pharmaceutical supply chains and the implementation of the new legislation requirements are set to dominate the industry for at least the next 5 years or more. This will add to the ever increasing burden on companies' audit systems and on the Qualified Persons who certify medicinal products for release.

NOTE: This Tech Talk on Supply Chain Assurance focuses on the start of the supply chain, ie purchasing of starting materials. Future Tech Talks will cover other aspects, eg Good Distribution Practice (GDP) and, when the Commission has decided how they will work, safety features.



NSF-DBA's training on Supply Chain 'Impact of US Initiatives and EU Falsified Medicines Directive' and 'Expectations and Regulatory Update on Anti-Counterfeiting Initiatives' will take place in our new offices October 15 and 16, 2013.

Quality Management and the OTC Sector

Casey Coy and Janeen Skutnik-Wilkinson review the current situation

In the previous Journal, we discussed the need for a third-party compliance and auditing tool to help OTC drug manufacturers comply with 21 CFR 210 & 211 and cGMP. Historically these products have been considered 'low risk'. However, if a manufacturer or their suppliers are not in compliance with cGMP and/or lack an effective quality system, including ingredients in the supply chain, they could be releasing ineffective or unsafe and potentially harmful products to the market. The Food and Drug Administration (FDA) lacks sufficient resource to inspect every drug manufacturing facility on a regular basis, so these types of 'low-risk' facilities are not inspected as often. The FDA has released several warning letters over the last 6 months that highlight some of the issues that are prevalent in this sector of the pharmaceutical industry.

On July 30, 2012 the FDA released a warning letter to Jiangsu Province Jianerkang Medical Dressing Co. http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2012/ucm314565.htm identifying significant violations of 21 CFR 210 & 211. According to the letter, the firm failed to establish and follow appropriate written procedures designed to prevent objectionable microorganisms in drug products not required to be sterile. The FDA collected and tested two lots of antiseptic wipe products that were intended to *"help prevent infection of minor cuts, scrapes and burns"* and were found contaminated with *Burkholderia cepecia*. The inspection revealed the facility failed to include in its written procedures validation of all sterilized processes, that are designed to prevent microbiological contamination of drug products purporting to be sterile. These issues were highlighted when the FDA identified that the company was not thoroughly performing Out-of-Specification (OOS) investigations for the failure of a batch or any of its components to meet its specification in addition to the lack of a stability testing program and identity testing of incoming raw materials and components.

On September 7, 2012 the FDA released a warning letter to Fercy Personal Care Products Co Ltd located in Zhejiang, China http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2012/ucm319504.htm identifying significant violations of cGMP. In addition to various OTC medical device and cosmetic products, Fercy manufactures and distributes OTC healthcare antiseptic products to the US market for private label hand sanitizers sold throughout numerous retail streams. The inspection identified a lack of written procedures describing the responsibilities and procedures applicable to the quality unit. The quality unit also failed to approve or reject drug product components, containers, closures, in-process materials, packaging material, labeling and finished products and procedures and specifications impacting the identity, strength, quality and purity of the drug product.

Most recently, on October 22, 2012 the FDA issued a warning letter to I Shay Cosmetics Inc, located in Gardena, CA http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2012/ucm327498.htm noting significant violations to 21 CFR 210 & 211. I Shay Cosmetics is a private label manufacturer and contract packager that manufactures products for skin and personal care and the professional salon markets. The most notable non-conformity identified that I Shay did not establish scientifically sound and appropriate specifications, standards, sampling plans and test procedures for their components and drug products. Other non-conformities identified included inadequate written procedures for production and process controls, inadequate cleaning procedures and processes and a lack of a stability testing program to ensure their products are stable throughout expiry. Finally, the firm was not performing identity testing on incoming raw materials and lacked a supplier qualification program. The facility was also manufacturing cough and chest congestion relief products that failed to meet the final monograph for Cold, Cough, Allergy, Bronchodilator, and Anti-asthmatic Drug Products for Over-the-Counter Human Use, 21 CFR Part 341 making them unapproved new drugs.

Reading through these warning letters and others, it is clear that there are OTC pharmaceutical firms which lack an effective quality system necessary for achieving overall compliance with cGMP for manufacture and supply of OTC drug products. With a lower frequency of inspections of these types of facilities, and the prevalence of private label manufacturers who fall into this category, it is no surprise that retailer pharmacies are concerned with the compliance and level of quality systems of their supply chain. To fill this need, NSF International is developing a new protocol, titled '*NSF P414-201x, Auditing Practices for the Assessment of the Manufacture of Over-the-Counter (OTC) Drugs*' against established GMP Standards, to help manufacturers understand which requirements must be met in order to produce OTC drugs. The new NSF regulatory-based protocol focuses on quality management and provides companies outsourcing manufacturing of drug products, including pharmacy retailers and others, with a means to qualify their pharmaceutical vendors and suppliers. The protocol in development will be reviewed by an expert panel and available for certification against in 2013.

NSF-DBA's auditors and consultants have been auditing the pharmaceutical industry's quality and manufacturing operations for more than 25 years. We have experience in identifying gaps companies may have against the regulations, while also providing guidance on how to remediate any potential non-conformances. Our auditors can provide a variety of auditing services, including a standard check list-style audit, a full week consultative-type audit and a mock FDA audit. Our auditing and consulting professionals have decades of auditing experience and the expertise to perform audits for any type of activity within the pharmaceutical and medical device industries.

Don't get left behind as the scrutiny over OTC drug product manufacture and ingredient supply chain increases! Contact Casey Coy or Janeen Skutnik-Wilkinson in our Boston Office for advice or to schedule your consultancy and/or auditing needs.

Casey Coy
Partner
Tel: **857-350-4788**

Janeen Skutnik-Wilkinson
Partner
Tel: **857-277-0060**

Industry News

USA News

FDA Organization

In September 2012 the FDA announced that it is planning to reorganize its Office of Regulatory Affairs (ORA), including creating new offices and reorganizing others, as it takes steps to remove cumbersome domestic and international distinctions and to keep up with increasingly global operations. The restructuring will also better position the ORA to address new legislative authorities included in the FDA Safety and Innovation Act (FDASIA).

In addition, CDER is looking to elevate the Office of Generic Drugs (OGD) into a 'super' office, a move necessitated by the recent passing of the Generic Drug User Fee Amendments (GDUFA) and a heightened US public focus on generic medicines.

The Food and Drug Administration Safety and Innovation Act (FDASIA)

The FDASIA was passed out of the US Congress on June 26, 2012. This new Act includes several major changes that will impact the pharmaceutical industry.

The FDASIA gives FDA the authority to collect user fees from industry to fund reviews of innovator drugs, medical devices, generic drugs and biosimilar biologics. It also reauthorizes two programs that encourage pediatric drug development. This Act reauthorizes the Prescription Drug User Fee Act (PDUFA), first enacted in 1992, and extends the scope of user fees to include generic drugs and biosimilar biologics for the first time.

There are two notable absences from the new FDASIA: one is that FDA was not given the authority that they sought from Congress to be able to order recalls, and the second is that there is no reference to 'track and trace'. However, on October 25 this year the US Senate's Health Education Labor and Pensions (HELP) Committee released a track and trace draft proposal. The proposal, if enacted, would give FDA the authority to work with industry to develop a national track and trace system.

As far as pharmaceutical manufacturers are concerned the section of the FDASIA that will have the greatest impact is Title VII, which is devoted to supply chain management. The main provisions of this title are:

- Removal of the requirement for biennial inspection of drug manufacturing sites and transition to a risk-based inspection frequency
- GMP now requires *"...managing the risk of and establishing the safety of raw materials used in the manufacturing of drugs, and finished drug products"*. Thus, failure to adequately control the supply chain of raw materials that are used in drug manufacture could result in the product being deemed adulterated
- FDA must establish good importer practices *"that specify the measures an importer shall take to ensure imported drugs are in compliance with the requirements of this Act and the Public Health Service Act"*
- Import of drugs will be barred if the manufacturer delays, denies, or limits an inspection, or refuses to permit entry or inspection
- Allows FDA to detain, for a certain period of time, any drugs found during an inspection that were thought to be adulterated or misbranded

EU Pharma News

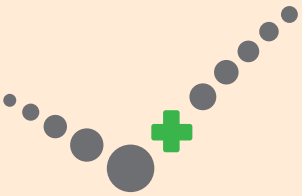
Falsified Medicines Directive – API Importation

Concerns over the implementation of the requirement that APIs imported from outside of the EU be accompanied by a certificate confirming compliance with EU GMP from the exporting country's Competent Authority continue to grow. Even the EU's ICH partners America and Japan appear to be reluctant to issue these certificates. We wonder whether European regulators truly understand that, unless they soften their demands regarding GMP certification of active ingredients, in six months' time many EU pharmaceutical companies will be out of business and the EU will be facing a catastrophic shortage of essential medicines.

Falsified Medicines Directive – Sales at a Distance (Internet Sales)

There is a whole range of new legal requirements governing what is called 'sales at a distance to the public', primarily aimed at controlling internet sales of medicinal products. One measure being introduced is a logo for approved internet sites.

On October 17, 2012 the Commission published a Concept Paper on the proposed internet controls. This provided two options for the proposed logo:



Good Pharmacovigilance Practice (GVP) Guidance

The EMA published the first batch of seven modules of GVP in June 2012, after a public consultation period from February to April 2012. It released modules III and X for consultation in June 2012 and modules IV and XV in July 2012. The full set of 16 final modules is scheduled to be available by early 2013.

The remaining five draft modules of the GVP package are under development and were scheduled for release for an eight-week public consultation during the fourth quarter of 2012.

- Allows FDA to take into account the inspections of a trusted foreign government when considering the risk of an establishment
- Requires commercial drug importers to register with FDA and submit a unique identifier for the principal place of business at the time of registration
- Greater penalties for counterfeiting drugs
  - 20 years' imprisonment or fine up to $1,000,000, or both
- Extraterritorial jurisdiction over any violation of the Federal Food, Drug and Cosmetic Act related to any article regulated under this Act if the article was intended to be imported into the US or if any act in furtherance of the violation was committed in the US

Some of the other changes introduced by Title VII FDASIA are:

- Company's drug listing to contain the name and place of business of each excipient manufacturer, including all establishments used in the production of the excipient, the unique facility identifier of each excipient establishment, and a point of contact mail address for each such excipient manufacturer
- For two years after the Secretary specifies a unique facility identifier system, the Secretary must maintain an electronic database. The database must allow FDA personnel the ability to search by any field of information or combination of fields submitted in a registration. The database must link to other relevant FDA databases
- Notification to FDA is required by a regulated person if the regulated person knows:
  - that use of a drug may result in serious injury or death
  - that there is a significant loss or known theft of such drug intended for use in the US
  - that the drug has been/is being counterfeited and the counterfeit product is in commerce in the US or could reasonably be expected to be introduced into commerce in the US, or the drug has been or is being imported into the US or may reasonably be expected to be offered for import into the US

In order to implement the FDASIA a number of FDA Rules and Guidances will need to be issued over the next few years, some of which have specified due dates, as listed below:

- Five Rules
  - Excipient information – no timeframe specified
  - Administrative destruction – final rule by July 9, 2014
  - Administrative detention – final rule by July 9, 2014
  - Standards of admission for imported drugs – final rule by January 9, 2014
  - Registration of commercial importers/GIPs – final rule by July 9, 2015
- Three Guidances
  - Specifying the Unique Facility Identifier (UFI) – no timeframe
  - Notification – no timeframe
  - Meaning of delay, limit, deny, refuse – guidance by July 9, 2013

EU GMP Guide Part 1

Revision of Chapter 1

The EU published the final version of the revision of Chapter 1 of Part I of the EU GMP Guide in September 2012 and it is effective from January 31, 2013.

The title of Chapter 1 has been changed to 'Pharmaceutical Quality Systems' in order to integrate with the principles described in ICH Q10, which is published in Part III of the EU GMP Guide.

The draft changes issued in 2009 included numerous direct quotes from ICH Q10, but these are not included in the final version. However, it should be noted that by adding new requirements to Chapter 1 it will make them apply to veterinary medicinal products, as well as human products, in the EU, even though ICH Q10 has not been adopted by VICH.

The main changes in the revised Chapter 1 are in the areas of:

- The Pharmaceutical Quality System
- Continuous improvement and change management
- Supply chain management
- Senior management responsibilities
- Deviations and CAPA

The revised Chapter contains an extensive list of items that the Pharmaceutical Quality System (PQS) should ensure. Some of these items were listed in the previous version under the Quality Assurance section, but there are several new items that the PQS should ensure.

The new Chapter 1 states that *"Senior management has the ultimate responsibility to ensure an effective PQS is in place … senior management's leadership and active participation in the PQS is essential"*.

The need for periodic management review, with the involvement of senior management, is specified.

The final PQS expectation is that *"The Pharmaceutical Quality Systems should be defined and documented. A Quality Manual or equivalent documentation should be established and should contain a description of the quality management system including management responsibilities"*.

The list of basic GMP requirements also has some additions:

- Significant deviations are fully recorded, investigated with the objective of determining the root cause and appropriate corrective and preventive action implemented
- The distribution of products should take account of Good Distribution Practices

Together these changes are significant, but if a company has already made changes to their quality management systems to meet ICH Q10 then they should already comply with most of the new Chapter 1.

Revised Chapter 7 (Outsourced Activities)

In September 2012 the European Commission published the final version of the revision to this Chapter. The title of this Chapter has been changed from 'Contract Manufacture and Analysis' to 'Outsourced Activities', broadening it to cover any outsourced activity that, if performed in-house, is covered by the GMP Guide. The revised version will become effective on January 31, 2013.

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 7.8 states *"The Contract Giver should be responsible for reviewing and assessing the records and the results related to the outsourced activities. He should also ensure, either by himself, or based on the confirmation of the Contract Acceptor's Qualified Person, that all products and materials delivered to him by the Contract Acceptor have been processed in accordance with GMP and the marketing authorisation".*

Annex 2: Biological Products

After issuing two draft versions since 2007 the final version was eventually published on September 6, 2012. This revised version is effective from January 31, 2013.

The original published version of Annex 2 was an anodyne document, rarely referenced by people in the field and long overdue for revision. The latest draft is a major revision, offering sound, practical guidance in most areas, and regular observation on the applicability of risk-managed decision making. Specific changes include:

- The guidance now takes account of the existence of Part II of EudraLex Volume 4 – GMP for active substances, which addresses the manufacture of bulk biological products
- The range of regulated biological products has increased significantly since publication of the current Annex and guidance on 'selected product types' has been included in the revision
- Recent regulation on advanced therapies required the preparation of specific guidelines for so-called 'Advanced Therapy Medicinal Products' (ATMPs)
  - Gene therapy products
  - Somatic cell therapy products
  - Tissue engineered products

The Scope, Principles and Part A reflect the structure of the original Annex 2, with updated guidance. Part B, the specific guidance, is a major change (and for the most part an improvement) to the structure and content of the Annex.

EU-Israel ACAA

On October 23, 2012 the European Parliament voted 379-230 with 41 abstaining in support of the Agreement on Conformity Assessment and Acceptance of Industrial Products (ACAA) between the EU and Israel. Medicinal products certified in the EU will be considered certified in Israel and vice versa under this, which is a protocol to the 1995 EU-Israel Association Agreement. It will apply to all pharmaceuticals except for advanced therapy products, special medicinal products based on tissues and cells of human origin, and medicinal products that include blood products.

An ACAA is a 'super' MRA, so may mean that imports from Israel will be able to be exempt from the need for re-testing on importation. The implementation date for this ACAA is not yet known.

ICH News

A Concept Paper is being prepared to justify the need to revise ICH Q7, the GMP Guide for Active Pharmaceutical Ingredients, APIs.

PIC/S News

Japan and Korea have applied to join PIC/S.

At the PIC/S committee meeting in May 2012 Indonesia became the 41st member of PIC/S.

At this meeting several key decisions were made. One was to introduce a new sub-committee structure, which will be implemented by January 1, 2014. The second important decision was to establish new Working Groups in order to explore how to develop some new projects with the following objectives:

- Extending PIC/S' mandate to new activities such as Good Clinical Practices (GCP) and Good Pharmacovigilance Practices (GPP)
- Creating a PIC/S Inspectorate Academy to provide cost-efficient, primarily web-based, high quality harmonized training for Inspectorates

UK News

The legal framework for medicines legislation in the UK has undergone a major revision, with most of the 1968 Medicines Act disappearing. SI: 2012 No. 1916 'The Human Medicines Regulation 2012' (issued under the European Communities Act 1972) has been published and became effective on August 14, 2012.

On October 18, 2012 the MHRA published a consultation paper, MLX 379, on the transposition of Directive 2011/62/EU ('the Falsified Medicines Directive') into UK legislation. This document posed some 69 questions with responses sent to the MHRA by November 19, 2012. The consultation paper was accompanied by an 'Impact Assessment'.

NSF-DBA US Office Expands – Introducing our US Office Team

We first opened our US office in Boston in 2008 – this now feels a long time ago to some of us!

Since then we have seen the US business continue to grow, creating strong links in the US pharmaceutical industry. We have become an integral part of the NSF Health Sciences division. 2012 has seen a lot of positive changes – we moved to our new offices and training facility in South Street, Boston, in the summer and expanded the NSF-DBA team significantly – both at staff level and our pool of US associates.

Now that we are settled into these offices we felt it about time that we update our customers and introduce you to our staff. We will provide an update on our associate pool in the next edition of the Journal.

Neil Wilkinson – Senior Partner

Neil has been with NSF-DBA since 2008, initially based in the UK office before joining Jim in Boston in 2009. Neil worked in the Pharma sector for 30 years, with increasingly senior roles in Quality, Manufacturing and Supply Chain, working at both site and global levels. Neil acted as a Qualified Person during his time with AstraZeneca. He also worked extensively with the trade associations and regulators in the US and Europe, and was the EU industry topic leader for ICH Q10 Pharmaceutical Quality System. Within NSF-DBA he leads the US office, undertakes business development and key client liaison, whilst also tutoring at our courses and in-house Quality Professional Programs.

Jim Morris – Partner

Jim was the initial member of the US team, joining us in 2008 and helping set up the US business. Jim has worked in the Pharma/Biotech sector for 25 years at Pfizer, Cilag and Mass Bio in plant operations and Quality roles. He has international experience with spells in Italy, Switzerland and Puerto Rico. Jim's key roles in the US office include business development and key client liaison, as well as administering the US Quality Leadership Program (QLP).

Casey Coy – Partner

Casey came to NSF-DBA from the Dietary Supplements part of NSF Health Sciences, relocating from the NSF HQ in Ann Arbor to Boston in 2011. She brings her significant knowledge of public standards setting, certification and audit programs, and laboratory activities from NSF Health Sciences and other NSF divisions. Casey is playing a key role in developing standards and programs to support our OTC Drug and Excipient services.

Janeen Skutnik-Wilkinson – Partner

Janeen is our newest partner, joining NSF-DBA in October 2012. She is very well known in the global Pharma/Biotech sector. Her industry experience was gained with Merck and Pfizer, with international experience working in Belgium and the UK. Janeen has also worked extensively with several trade associations, FDA, other key global regulators, and within ICH for many years. Janeen has been Chair of IPEC and currently chairs the IPEC Federation. As well as her work for NSF-DBA, Janeen will be working on the integration of NSF Health Sciences and advocacy.

Austin Caudle – Business Development Manager

Austin joined NSF-DBA in 2012 as our first dedicated business development professional. He joined us from Charles River and has a strong technical background in the Pharma, Biotech and Medical Device sectors to complement his business development skills. As NSF-DBA continues to grow, Austin will help us to build, sustain and develop client relationships with firms and individuals, and identify areas of new business.

Kate Principe – Lead Administrator

Kate joined the US team in 2011, after many years working at Liberty Mutual at executive assistant level. Kate has since become a major driving force within our US office. Kate leads the administration team activities and liaison with our other offices, as well as playing a key role in client liaison for a number of our key programs.

Sarah Gleason – Administrative Assistant

Sarah joined NSF-DBA in 2012 having had previous experience in Human Resources at the New York Times and executive assistant experience roles in healthcare companies.

Jefferson Norville – Administrative Assistant

Jeff is the latest addition to the administration team, joining us in September 2012. Jeff has experience and a major interest in healthcare science as well as experience in administration activities.

So a hearty hello from all of us in the NSF-DBA US office in Boston – a true mix of New Englanders, 'Old Englanders', and a little bit of mid-west and the south too! Diversity makes a great team!

Forthcoming Pharmaceutical Courses

What's planned for February – May 2013

Pharmaceutical Packaging

Boston Marriott Cambridge, Cambridge, MA
February 5 – 7

Despite advances in technology, quality problems with packaging still continue to occur. Print origination and packaging processes continue to be a major reason for product recall!

This course has been carefully designed to cover all important aspects of the packaging process, from selection of suitable components, pack design, packaging processes and their associated GMP challenges, through the supply chain to the patient.

The course includes visits to a wholesaler and a pharmacy, with input from printed packaging component suppliers. The course aims to provide the necessary understanding of packaging materials and the packaging process to enable the quality professional to carry out his/her duties with knowledge. Equally, the course will be of value to staff involved in packaging development, packing operations, QA and QC.

Course Fee: **$2950.00** (First booking)
$2360.00 (Early bird/additional bookings from same site)

Workshop: Facilities and Utilities (for Biopharmaceutical Operations)

NSF-DBA Boston Office, Boston, MA
February 26

HVAC for Biopharmaceutical Facilities
Morning Session 08:30 – 12:00

This half-day 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. Hand-outs and slides will be a valuable reference tool.

Clean Utilities for Biopharmaceutical Facilities
Afternoon Session 13:00 – 16:30

In the afternoon 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

Extractables & Leachables Requirements in Pharmaceutical Development

Minneapolis Marriott City Center, Minneapolis, MN
March 5

San Mateo San Francisco Airport Marriott, San Mateo, CA
March 7

This course will review the Extractables and Leachables (E&L) arena and describe the strategies leading companies are taking to evaluate, test and document the E&L studies for primary and secondary packaging. The course will cover the types of extractables expected from typical packaging and devices as well as the PQRI recommended 'best practices' for conducting E&L studies. An overview of current methods and test protocols will be provided. Current analytical challenges, case studies and regulatory concerns will be reviewed.

Course Fee: **$950.00** (First booking)
$760.00 (Early bird/additional bookings from same site)

Quality Management Systems

Boston Marriott Cambridge, Cambridge, MA
April 10 – 12

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 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!

This course will provide you with answers to the really tough questions you have to deal with day-to-day, such as:

- How to design a Quality System that is fast, flexible, simple and compliant
- How to ensure that your system remains fully compliant no matter how tough the business environment
- How to accurately measure and continuously improve your Quality System

Course Fee: **$2950.00** (First booking)
$2360.00 (Early bird/additional bookings from same site)

Book online at www.nsf-dba.com

Get in touch now to book your place on any of these courses
Call us on: +1 857-277-0060 or email: USinfo@nsf-dba.com

NSF DBA℠
The Health Sciences, Training, Consultancy and Auditing Experts

Workshop: Laboratory GMP Requirements and Investigating Out of Specification Results

NSF-DBA Boston Office, Boston, MA

May 16

Laboratory GMP Requirements
Morning Session 08:30 – 12:00

This short course will provide an overview of GMP expectations of the pharmaceutical laboratory and common areas of weakness cited by regulators – data management, sample management and best practices. Differences between laboratories supporting clinical operations versus commercial operations are highlighted. Your tutor will share his experience of global laboratory management and Process Analytical Technology applications.

Investigating Out of Specification Results
Afternoon Session 13:00 – 16:30

The management of Out of Specification (OOS) results is a critical aspect of laboratory operations. Frequently, OOS procedures are difficult to follow, leading to skipped steps and data gaps. This course will review best practices and system weaknesses frequently encountered. The history and background of current OOS guidelines will be covered by your tutor. Attendees will realize that to meet the requirements of the Equilibration Time and Bowie and Dick test, the cycle must be highly efficient. The efficient cycle has the knock-on effect of being relatively short, ie 1.5 hours as against 4+ hours and therefore the impact of this approach is highly significant in an operational sense as well as from a quality perspective.

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

Our workshops are designed to give you practical examples of key pharmaceutical areas. These will be ideal for those people looking for ways to operate more compliantly and effectively.

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 changes which may become necessary.

Jim Morris discusses changes in the FDA after attending the PDA/FDA conference earlier this year

FDA speaker, Dr Steve Solomon's, keynote remarks at this year's PDA/FDA conference reflect the dramatic changes in the global pharmaceutical marketplace. He noted a quadrupling of shipments into the US from 2002 to 2012; additionally, 40% of finished product and 80% of APIs are imported from foreign sources. The FDA has responded as a health agency prepared for global supply by establishing offices on nearly every continent including three posts in China and two posts in India. Their stated goals are to increase collaboration with regional and national regulatory counterparts, get to know the exporters, and help transfer FDA standards outside the US. Furthermore foreign inspections by the FDA have more than doubled in the three year period from 945 inspections in 2008 to 2,217 inspections in 2011. The offices of Regulatory Affairs and Office of International Programs are now being combined into the Office of Global Operations and Policy under Deborah Autor. The mission of this new office is to maximize import safety, integration of international programs within the FDA, and policy implementation to address global operations.

Clearly the FDA is adjusting its approach to protecting US consumers. Yet with FDA regulated products supplied from 150 countries and 300,000 manufacturing sites the FDA's success is going to be a function of collaboration and education. Ultimately responsibility for product quality and supply chain integrity will continue to rest with the license holder of the pharmaceutical product and/or medical device.

The European Medicines Authority is similarly responding to the changing global landscape and increased threat of Heparin type incidents with the introduction of the Falsified Medicines Act. In true European fashion, responsibility will be delegated to the member states and ultimately rest with the license holder. And EMA expectations of the Qualified Person continue to notch up another level.

The FDA and EMA are following predictable pathways to protecting public health; the FDA extending its reach to the degree possible and EMA largely delegating responsibility to member states, license holders and their Qualified Persons. Where does the true answer lie to a safe borderless marketplace for pharmaceuticals? At NSF-DBA we would favor collaboration between agencies and not-for-profit organizations such as PIC/S and Rx-360, and while accountability will always ultimately rest with the license holder, we will strongly advocate the preparation and training of the key decision makers and personnel involved in GMP operations throughout the supply chain. While surveillance and oversight is an important part of the formula, the value of preparation and training cannot be overstated.

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Meningitis Outbreak – *Where does the Fault Lie?*

By Jim Morris

Exserohilum rostratum is the organism recovered from three lots including unopened vials produced at the New England Compounding Center (NECC) in Framingham, Massachusetts. It is a plant eating fungus favoring tropical to subtropical climates and often found digesting grasses. A characteristic of this organism is its ability to 'launch' its spores airborne. How did this organism or its spores find their way into the NECC and the production of preservative-free methylprednisolone acetate? This is certainly one of the questions being investigated by the FDA and CDC. But unfortunately at this point this question is largely academic, and more fundamental questions concern the lack of internal and external oversight of this company and perhaps others like it in the US.

Scientific American © Glenn Roberts

Those involved in the production of sterile medicinal products know first-hand how demanding and rigorous sterile manufacturing operations must be day in and day out. Personnel at all levels must be exceedingly well trained and support staff, including engineering, maintenance, quality control and validation, all have an incredibly important role to play.

As in past drug related tragedies, this one is likely to trigger new legislation. And while there is a tendency to find blame, this case will come down to systemic failures inside and outside the company.

Product quality and patient safety are not only functions of the quality systems in place but are also functions of company leadership. This investigation points to lapses in leadership decisions at NECC. Therefore, one question that should be taken up is the independent role of quality in companies like NECC and who at NECC routinely makes critical product quality decisions. In many countries, facilities licensed for manufacturing activity similar to that performed by NECC would have required the presence of a Qualified Person whose responsibility goes beyond that of the company and extends to both patients and regulators. The role, when established, ensures the focus on systems and processes that lead to GMP, supporting all of the quality systems and the people who work with them. Had this role been in place at NECC, in all likelihood this tragedy could have been averted.

Our course on Quality Management Systems will be held April 10-12, 2013 in Cambridge – do not miss this opportunity to learn how to reinforce your QMS

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