Excipient GMP GDP Certification Project

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Excipient GMP GDP and Certification

1. Basis for Project
2. Certification Project Structure
   1. Classification
   2. GMP
   3. GDP
   4. Auditor Competency
   5. Advocacy and Publicity
Why Certification?

• The last presentation asked the same question for Cosmetic Ingredients – the same reasons apply to Pharmaceutical Excipients
  AND
• Excipients pose a finite but small risk to the patient
• That risk is controlled by the excipient supplier through adoption of GMP and GDP (but it’s not a legal requirement to do this) or by the pharmaceutical user.
• If either sets of controls are compromised then this risk can be realised
• Pharmaceutical user Audits are important but infrequent.
• UK MHRA survey reported
  • Over 1200 excipients in use in marketed pharmaceutical products (not including colours and flavours)
• Can Regulators inspect all excipient suppliers?
• Can users?
Difficulties and Challenges in Regulating Excipients

• It’s not all GMP – As tragedies events continually show us – what happens between the excipient Supplier and the User is as critical if not more so!

• GDP has to be central stage as well

• Recent signals from the EU and FDA have indicated that:
  – 3rd Part Excipient Audits and Certification have a role to play
  – For APIs The December 2008 Pharmaceutical Package from the EU expressly required this
Excipients GMP GDP Certification Project

- EFCG promoted the development of a global task force to provide a solution which led to a MOU with IPEC Europe in May 2008
- GMP and GDP Certification is a daunting task and even IPEC or EFCG alone cannot hope to deliver a global solution
- The project scope requires the partners to contribute their collective experience and expertise
- IPEC Europe and EFCG Partners now include:
  - FECC – European Association of Chemical Distributors
  - IPEC-Americas
  - PQG - Pharmaceutical Quality Group
Experience with GMP Certification so far

• Past Experience with PQG PS 9100
  – Use ISO 9001 type auditing and certification
  – Only 2 certificates have been issued - both in the UK
• IPEA - International Pharmaceutical Excipients Auditing Inc
  – Uses expert audit report (comparable with regulatory inspection)
  – More uptake than PS 9100 and worldwide in scope
• EFfCI GMP Guide for Cosmetic Ingredients
  – Scheme launched November 2008 – ISO 9001 type certification
  – NB IPEC-PQG GMP Guide is 80% identical to the EFfCI GMP Guide
• Use experiences of these to build Excipients Certification programme
European Excipients Certification Project

Key Deliverables of the Project:
- International in scope
- Based on the IPEC-PQG GMP Guide 2006
- Based on IPEC GDP Guide 2006
- Aligned to ISO 9001 (2000 and 2008 editions)
  - Many excipient suppliers are already ISO certified

Key Project Principles:
- Evolve existing best practices from all known sectors
- Classify excipients
- Must include GDP and GMP
- Auditor training and competency requirements must be defined
- The scheme must apply to the majority of the existing excipient industry without raising the bar too high
Excipient GMP GDP and Certification

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Excipient Classification

Lead Members: EFCG - IPEC Europe  IPEC-Americas

• Why classify Excipients?
  – They have many diverse uses, functions, manufacturing processes and origins
  – So the risks posed to the patient are also very variable
  – Hence a one size fits all definition of GMP is not going to be enough

• Higher risks require more extensive controls over excipient consistency, process and contamination controls, notification of changes etc. than defined in the IPEC-PQG GMP Guide
Excipient Classification

• “One size will not fit all”

• Aim to align with ICH Q7 / EU GMP for very high risks
Excipient Classification

- The classification will define the extent of GMP required,
  - Recent survey conducted by IPEC Europe to see what users and suppliers in the trade associations thought about this concept
  - Data being analysed but in agreement with:
    - The IPEC-PQG GMP Guide will be the foundation (class 1)
    - The highest class (3) should not exceed EU Part II / ICH Q7 GMP
    - An intermediate class (2) between these should be defined
      - The investment in the quality management system between the IPEC-PQG GMP Guide and EU Part II is very high
      - Man decades of work on a multi purpose site
Excipient Classification

- Expectation that the majority of excipients will match the existing IPEC-PQG GMP Guide

Proportion of Excipients by Classification

- IPEC-PQG GMP Guide
- Class 2
- Class 3
Excipient Classification

Classification process in 3 Phases
1. Manufacturer to perform risk assessment, and so determine class of GMP
   • Supplier to communicate GMP class to Suppliers and Users (e.g. on CofA)
2. User to perform risk assessment and request GMP class from supplier
   • User to communicate GMP class to suppliers at contract review
3. User and Supplier to perform joint risk assessment
   • Best option, but may not always be practical due to numbers of customers (1000s) and number of excipients (1000s)
   • BUT an agreement at least on the GMP class must be part of contract review between the two parties
Key elements of the Classification risk assessments

1. Known functionality characteristics of the excipient
2. Known uses of the excipient including route of Administration
3. Origin of the excipient (animal, vegetable, mineral)
4. Manufacturing process / Multi purpose plant
5. .....
Lead Members: PQG, IPEC Europe, IPEC-Americas

First Phase GMP Certification

- Will Use the IPEC-PQG GMP Guide 2006
- An Annex to ISO 9001:2008 will be prepared that places additional auditable requirements on a supplier
- Some aspects of the current Guide have been made compulsory as a result
- Enhanced GMP requirements for the other classes of excipients have been developed
  - A draft of the base GMP and the enhanced requirements are available for comment
Excipient GMP

• Aim of this aspect is to transform the IPEC-GMP Guide into an ISO 9001 type standard
• ISO 9001 and related Pharmaceutical Packaging (ISO 15738) and Medical Device (ISO 13485) auditors can then be trained to conduct audits of suppliers against these requirements
• Allows access to a large and international pool of auditors
• Later Phases of GMP Certification
  – There will be a need to revise the 2006 GMP Guide so that the additional requirements for the different classes of excipients have suitable guidance for suppliers and user
• Good Distribution Practices are essential as recent tragedies in 2006 and 2007 have illustrated
• IPEC GDP Guide 2006 built on the WHO GDTP Guide 2003 and integrated with good transportation practices for chemicals
• Excellent uptake of GDP in Certain Excipients Consultation
Excipient GDP

Lead Members: FECC, IPEC Europe, IPEC-Americas

GDP is a critical component, as recent events have illustrated

- GDP Audit Guide is aligned with the European SQAS ESAD II assessment scheme (www.sqas.org)
  - Which is already subject to independent assessment
  - And has a defined auditor training programme
  - Therefore build on this structure and system to deliver GDP certification using the enhanced definitions of Auditor competency
GDP Standard and Annexes

Key Stages

- Matched to fit the activities of the supply chain
- See current GDP Guide for details
- The GDP aspects should be capable of being audited separately from the GMP part – to distinguish between those organisations who are uniquely distributors or manufacturers
- An Annex to ISO 9001:2008 needs to be developed which sets out the requirements in the GDP Guide. This is more difficult than for the GMP Guide as the GDP guide is not already aligned to the ISO 9001 section headings
Lead Members: To be defined

Where do we find all the auditors?

• Given the numbers of excipient suppliers
• Given the global reach of certification, mirroring the supply chain
• Who has enough auditors to perform frequent, at least annual audits of suppliers?
• Inspectorates? Users? Other similar bodies? IPEA?
• ISO 9001 pharmaceutical industry auditors?
  – Potentially 1000s of these
  – Well developed and policed accreditation infrastructure
  – Already perform medical device audits
Auditor Competency

- Regulators have consistently stated they have concerns about auditor competency and their ability to perform effective GMP audits
  - Hence project will deliver auditor competency criteria and ensure that auditors are trained in these requirements
- EU December 2008 Pharmaceutical Package stated that:
  - The user must verify compliance to GMP/GDP by themselves or through a body accredited for that purpose by the competent authority of a Member State.
  - But applies to APIs only (excipients are not mentioned in this draft Directive)
- The die is cast
Auditor Competency requirements
• Will cover GMP and GDP aspects
• Need to access as many auditors as possible
• Training materials will be made available for auditors
• To further enhance matters in this area an individual auditor accreditation system is desirable
• It will define auditor competency and pedigree
• European regulators invited and agreed to participate
• What else do we require on this topic?
Excipient GMP & GDP Certification

Lead Members: To be defined

Certification Plans

• Two certificates will be available
  – An ISO 9001 type certificate will be available from those ISO 9001 certification bodies who meet the training and competency requirements to their auditors – European Team
  – IPEA will obtain ANSI accreditation status thereby putting it on a par with other accreditation bodies and IPEA will supply an expert Audit report “certificate” – American Team

• Two options allows us to maximise benefits of the existing options without eliminating one or the other
  – Likely that ISO style certificate will be suitable for the majority of excipients and that the enhanced classes of excipients will use the export Audit report system
Excipient GMP & GDP Certification

How it works

• Balance all the players
• Suppliers – Users - Regulators
• Ensure a win-win-win situation is generated
Excipient GMP & GDP Certification

**Certification Plans**

- Supplier or User commissions 3rd Party
- Who is accredited by national competent authority
- Passes evidence of GMP and GDP to User
- Passes details to regulators at inspection or in dossiers
- Virtuous circle
Key requirements for Excipient GMP & GDP Certification

Virtuous Circle

• Could there be some kind of regulatory relief to users?
• Dare I dream of less user audits?
• **Publicity and Advocacy**
  - Presentation of scheme was given to EMEA Interested Parties meeting in London 26 November 2008
  - The scheme was observed as “Ambitious”
  - “A good idea” in that it will increase assurance of the pharmaceutical starting material supply

• **Details have been given to the FDA recently, feedback awaited**
Excipient GMP GDP and Certification

• Current Status
  – An ambitious project has been defined and launched
  – The key components have been defined
  – Task forces and their deliverables have been assembled and are making excellent progress
  – Participants have been invited and calls made to ask for volunteers
  – Feedback will be sought at key stages in the development of the project
None of this is realisable without the commitment and contribution of all the volunteers to the various working parties and the Steering Committee.

I thank them for all their efforts.

Thank you for your attention.