FORECASTED GUIDELINE CHANGES 2013

SAPRAA - Nov 2012

J Savrda

Quality Audit & Technical Executive

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SCOPE OF THE GAME

- ***"The fascinations of shooting as a sport, depends almost wholly on whether you are, at the right or wrong end of the GUN!"***
  - PG WODEHOUSE

REASON for FORECAST

PRESS RELEASES
2012 PIC/S MEETINGS
GENEVA, SWITZERLAND &
KIEV, UKRAINE

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21 May 2012
PRESS RELEASE PIC/S MEETINGS, Geneva

- **“Harmonisation of guidance documents**
- The PIC/S Committee adopted the new consultation procedure **“Harmonisation of PIC/S and EMA GMDP IWG Consultation Procedures”** between PIC/S and the European Medicines Agency (EMA) which will ensure further improvements in the **harmonisation** between the **EU and the PIC/S GMP Guides** and related documents.”

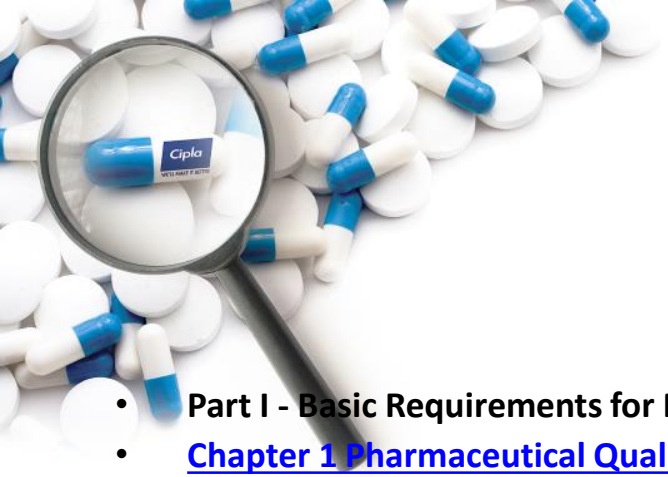
23 October 2012

PRESS RELEASE PIC/S MEETINGS, KIEV, UKRAINE

- "With respect to the project of extending PIC/S' mandate to new activities such as **Good Clinical Practices (GCP)** and **Good Pharmacovigilance Practices (GVP),** discussions had been carried out with the EMA Ad Hoc Working Groups on GCP and Pharmacovigilance."

EUROPEAN MEDICINES AGENCY

- What awaits us in 2013 in terms of:
- **GMP**
- **GDP**
- **GCP**
- **GVP**
- GLP

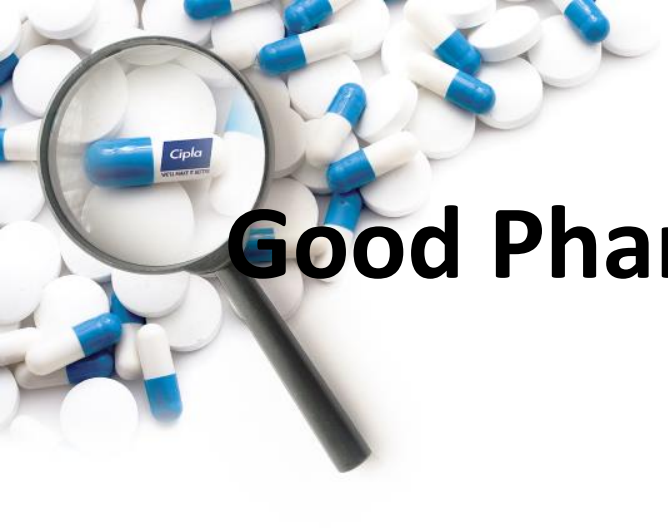


EMA GMP

- **Part I - Basic Requirements for Medicinal Products**
- **Chapter 1 Pharmaceutical Quality System (66 KB)**(Deadline for coming into operation: **31 January 2013**)
  Chapter 1 Quality Management (revision February 2008)(29 KB)
- Chapter 2 Personnel(20 KB)
- Chapter 3 Premise and Equipment(34 KB)
- Chapter 4 Documentation (Revision January 2011) - Coming into operation by 30 June 2011(33 KB)*NEW*
- Chapter 5 Production(50 KB)
- Chapter 6 Quality Control (33 KB)
- **Chapter 7 on Outsourced activities(21 KB)** (Deadline for coming into operation: **31 January 2013**)
  Chapter 7 Contract Manufacture and Analysis(22 KB)
- Chapter 8 Complaints and Product Recall (18 KB)
- Chapter 9 Self Inspection(11 KB)
- **Part II - Basic Requirements for Active Substances used as Starting Materials**
- Basic requirements for active substances used as starting materials(452 KB)
- **Part III - GMP related documents**
- Site Master File (33 KB)
- Q9 Quality Risk Management
- **Q10 Note for Guidance on Pharmaceutical Quality System**
- MRA Batch Certificate(101 KB)

ICH GUIDELINES

- Q7 - GMP for API manufacture Nov 2000
- Q8 - Pharma. Development Nov 2008
- Q9 - Quality Risk Management Nov 2005
- Q10 - Pharma. Quality Systems June 2008
- Q11 – Development & Manufacture of Drug Substances May 2012
- E 8&9 - Clinical trials 1997/8
- M4 series – CTD for registration Nov 2000



EMA
Good Pharmacovigilence Practise

- Rules Governing Medicinal Products in the European Union (chapter I.2 of Volume 9A for human products and in section 5 of the standalone guideline under Volume 9B for veterinary products).
- Refer ICH Conference in Oct 2012

CONSTANTLY CHANGING ENVIRONMENT

- 80% of the SUCCESS of world-class companies is due the
  - Excellence in Implementation and
  - Delivery under Various Conditions!!

- So who is Responsible to IMPLEMENT

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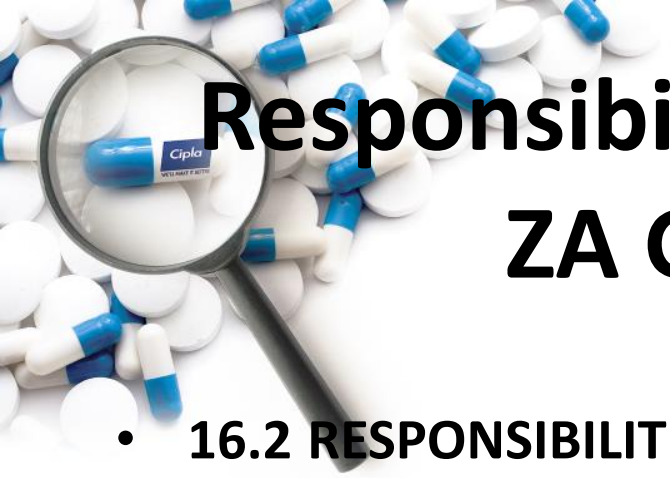
Responsibilities of key personnel – ZA GMP GUIDELINES



- **16.2 RESPONSIBILITIES OF KEY PERSONNEL**
- Key personnel include:
- **a natural person** who resides in South Africa responsible to the Medicines Control Council for compliance with the requirements of the Medicines and Related Substances Act, 1965 (Act 101 of 1965).
- the person responsible for **Production**,
- the person responsible for **Quality Assurance**, and
- the **Responsible Pharmacist** responsible to the -
- Medicines Control Council for compliance with the requirements of the Medicines and Related Substances Act, 1965 (**Act 101 of 1965**) and the
- Pharmacy Council for compliance with the requirements of the Pharmacy Act, 1974 (**Act 53 of 1974**)

INVESTIGATE

“In business the unexamined game is not worth playing”

CLEM SUNTER

Volume 4
EU Guidelines for Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use
Chapter 1
Pharmaceutical Quality System

January 2013 IMPLEMENTATION

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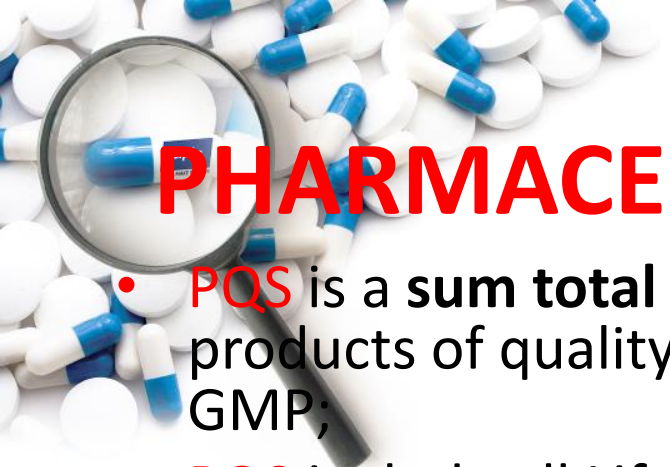

PHARMACEUTICAL QUALITY SYSTEM

- PQS is a **sum total** of organised arrangements to deliver products of quality required for intended use, thus including GMP;
- PQS include all Life-Cycle Stages – pharmaceutical development, manufacture of investigational meds, technology transfer, commercial manufacturing, discontinuation;
- PQS design needs to take into account size & complexity of the company's activities;
- PQS needs to ensure specific outcomes, details to follow;
- Senior Management has the ultimate responsibility of an effective PQS;
- Periodic Snr Management review of PQS to ensure continuous improvement;
- PQS should be defined & documented.

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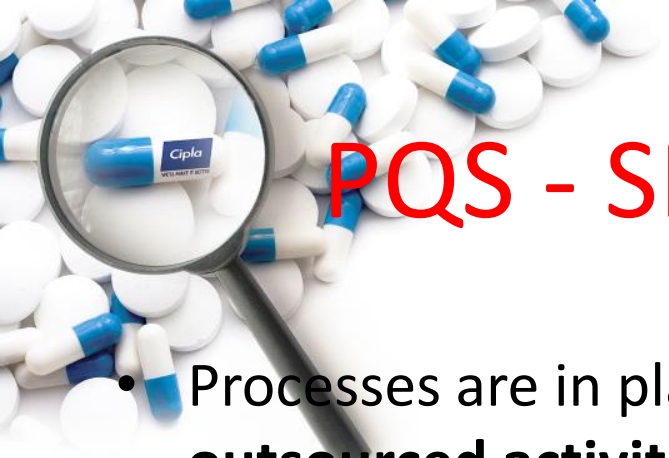
PQS - SPECIFIC OUTCOMES

- Ensure Consistent delivery of products with appropriate **quality** attributes;
- Product and process **knowledge is managed** throughout all lifecycle stages;
- Products are designed & developed in accordance with **GMP**; QbD
- Production and control **operations are clearly specified** and Good Manufacturing Practice applied;
- **Managerial responsibilities** are clearly specified;
- Manufacture, supply and use of the **correct** starting and packaging materials, the selection and monitoring of **suppliers** and verifying, that each delivery is from the approved supply chain;

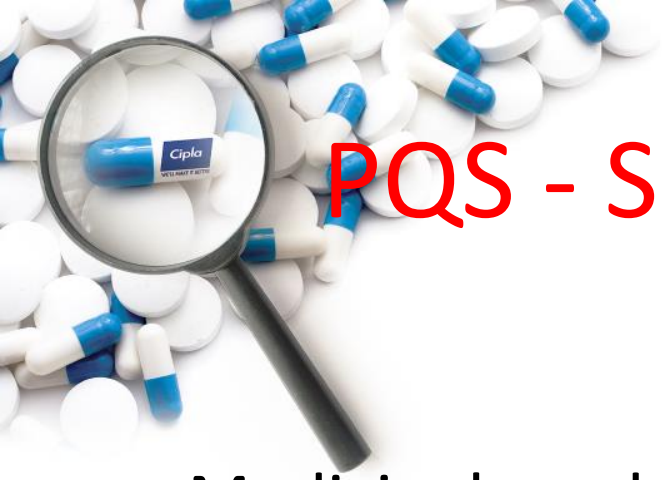


PQS - SPECIFIC OUTCOMES

- Processes are in place to assure the management of **outsourced activities**;
- A state of control is established and maintained by developing and using effective **monitoring and control systems** for process performance and product quality;
- The **results** of product and processes monitoring are taken into account in **batch release**, in the investigation of **deviations**, and, with a view to taking **preventive action** to avoid potential deviations occurring in the future;
- All necessary controls on **intermediate products**, and any other in-process controls and **validations** are carried out;

PQS - SPECIFIC OUTCOMES

- Continual improvement is facilitated through the implementation of **quality improvements**;
- Arrangements in place for **prospective** evaluation of planned **changes** and approval prior to implementation taking into account regulatory notification and approval where required;
- After **implementation** of **changes**, evaluation is undertaken to confirm that quality objectives were achieved and that there was no unintended deleterious impact on **product quality**; (AQR; Process Analytical Tech.)
- Appropriate levels of **root cause analysis** should be applied using **Quality Risk Management** principles;
- Responsible Pharmacist – **Batch Release**;



PQS - SPECIFIC OUTCOMES

- Medicinal products are **stored, distributed** and subsequently **handled** so that quality is maintained throughout their shelf life;
- **Self-inspection** and/or **quality audit**, which regularly appraises the effectiveness and applicability of the Pharmaceutical Quality System.

COMPLEXITY

- ***"I wouldn't give a fig for the simplicity this side of complexity, but I'd give my life for the simplicity on the far side of complexity!"***
  - Justice Oliver Wendell Holmes

Volume 4
EU Guidelines for Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use
Chapter 7
Outsourced Activities

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Outsourced Activities

- Any **activity** covered by the **GMP Guide** that is **outsourced** should be appropriately **defined**, **agreed** and **controlled** in order to **avoid** misunderstandings, which could result in a product or operation of **unsatisfactory quality**. There must be a **written** Contract between the Contract Giver and the Contract Acceptor which clearly establishes the duties of each party. The **Quality Management System** of the Contract Giver must clearly state the way that the Qualified Person certifying **each batch** of product for **release** exercises his full **responsibility**.

The Contract Giver (CG)

- The **PQS** of the CG should include the control and review of any outsourced activities. The CG is **ultimately responsible** to ensure processes are in place to assure the control of outsourced activities. These processes should incorporate **quality risk management;**
- **Prior** to outsource, CG is responsible for assessing the legality, suitability and the competence of the Contract Acceptor (CA) to carry out **successfully** the outsourced activities. The CG is also responsible for ensuring by means of the Contract, that the principles and guidelines of GMP are followed;
- The CG to provide the CA with all **information and knowledge** necessary to carry out the contracted operations **correctly** in accordance with regulations and the Marketing Authorisation (Registration) for the product concerned (Tech Transfer);

The Contract Giver (CG)

- CG to **monitor and review** the performance of the CA;
- CG to review and assess the **records** and the **results** related to the **outsourced activities**, to ensure all products and materials delivered to him by the CA have been **processed** in accordance with **GMP** and the **marketing authorisation (registration)**.

The Contract Acceptor (CA)

- The CA must be **able** having **adequate** premises, equipment, knowledge, experience, and **competent** personnel;
- CA to ensure that all products, materials and knowledge delivered to him are **suitable** for their **intended** purpose;
- CA should not **subcontract** to a third party any of the work entrusted to him by the Contract without the CG's prior evaluation and **approval**;
- CA not to make **unauthorized changes**, outside the terms of the Contract, which may adversely affect the quality of the outsourced activities;
- CA to understand that **outsourced activities**, including contract analysis, may be subject to **inspection** by the **competent authorities.**

DECISIONS

- *"No **sensible decision** can be made any longer without taking into account not only **the world as it is, but the world as it will be**!"*
  - Isaac Asimov

The Outsource Contract

- A Contract should specify the respective **responsibilities** and **communication** processes relating to the outsourced activities;
- **Technical** aspects of Contract to be drawn up by **competent** persons, suitably knowledgeable in related outsourced activities and **GMP**, in accordance with **regulations in force** and the Marketing Authorisation (Registration) for the product concerned;
- The Contract to describe clearly **who** undertakes **each step** of the outsourced activity, e.g. knowledge management, technology transfer, supply chain, subcontracting, quality and purchasing of materials, testing and releasing materials, production and quality controls (including in-process controls, sampling and analysis);

The Outsource Contract

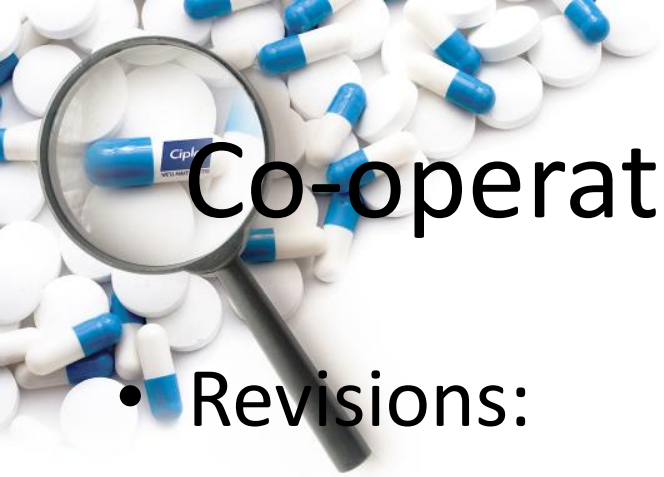
- All records related to the outsourced activities, e.g. manufacturing, analytical and distribution records, and reference samples, should be kept by, or be available to, the CG;
- The Contract should permit the CG to audit outsourced activities, performed by the CA or his mutually agreed subcontractors.

PLAYING THE GAME

THE FOUR SIMPLE ACTIVITIES

- **Tactics** – Planning by Snr Management;
- **Decisions** – Quality Risk Based: What, When, Why, Who, How Often;
- **Actions** – Deal with it, Document it,

  JUST DO IT
- **Outcomes – Measurable Outcomes!!!!**



Co-operation with non-EU states

- Revisions:
- Qualification and Validation – TGA, Canada, US FDA, HPFBI
- Parametric Release – Canada, HPBFI, US FDA
- Global Supply Chain and GMP Compliance – Canada
- Medicinal gases, Herbals, Biologicals, Blood & Plasma, Radiopharmaceuticals, etc

GROWTH

- New : New Zealand and Chinese Tipei/Taiwan
- Pre-Assention: Belarus and Uganda
- Re-assessment: Latvia, Lithuania
- Applicants: ANVISA, Japan, Korea, Philippines, Armenia, Mexico and China

THANK YOU