EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

GMP Issues for Start-Ups, quality in the supply chain and role of the Qualified Person (QP)

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Introduction

- EU GMPs – what and why?
- What does it mean for a start up
- Supply chain management
- Investigational Medicinal Products & Clinical trials
- Qualified Person

GMP-what its not?

Great

Mounds of

Paper

GMP – what it is?

GMP shall mean the part of quality assurance which ensures that products are consistently produced and controlled to the quality standards appropriate to their intended use

GMP- what is it

EN Official Journal of the European Communities

DIRECTIVE 2001/83/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 6 November 2001

on the Community code relating to medicinal products for human use

EN Official Journal of the European Communities

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(Acts whose publication is obligatory)

DIRECTIVE 2001/82/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 6 November 2001

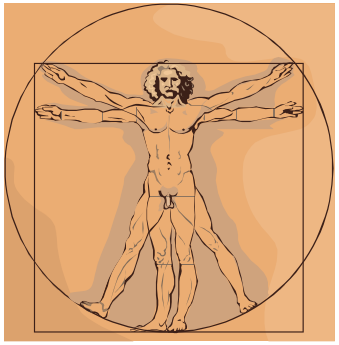
on the Community code relating to veterinary medicinal products

Article 40 -Member States shall take all appropriate measures to ensure that the manufacture of the medicinal products within their territory is subject to the holding of an authorization. This manufacturing authorization shall be required nothwithstanding that the medicinal products manufactured are intended for export

Article 44- Member States shall take all appropriate measures to ensure that the manufacture of veterinary medicinal products in their territory is subject to the holding of an authorization. This manufacturing authorization shall likewise be required for veterinary medicinal products intended for export.

GMP – what is it?

The rules governing medicinal products in the European Union contains guidance for the interpretation of the principles and guidelines of **good manufacturing practices** for medicinal products for human and veterinary use laid down in Commission Directive 2003/94/EC, and 91/412/EEC respectively.



GMP – what is it?

Good Manufacturing Practice

Part I	Part II	Part III	Annexes
Basic Requirements for Medicinal Products	Basic Requirements for Active Substances used as Starting Materials	GMP related documents	Substance specific documents
9 Chapters	1 Chapter(49pg)	5 documents	19 annexes

http://ec.europa.eu/health/documents/eudralex/vol-4/index_en.htm

GMP for SME

Quality System – Premises / Equipment / Materials

i. Facility designed

a. Process flows for staff, equipment, materials & reagent, product, waste etc;

b. Air quality, pressure differential defined, air flows

c. Fit for purpose

Pharma –Large / Small

University Based

Hospital Based

GMP for SME

Quality System – Premises / Equipment / Materials

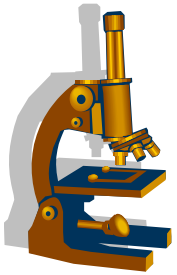
ii. Reagents / Materials

a. Fit for purpose

b. validation / qualification

c. Quality of reagents – No Laboratory / Reagent grade

d. Batch acceptance of reagents



GMP for SME

Quality System -Documentation

a. Need to have process defined

b. Need to have procedures defined

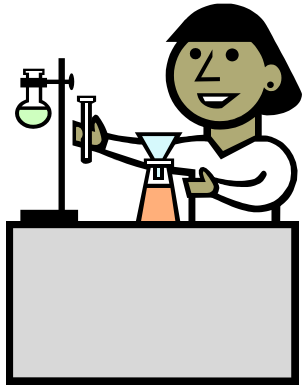
c. Appropriate forms / means for recording data to demonstrate consistency with defined process / procedures

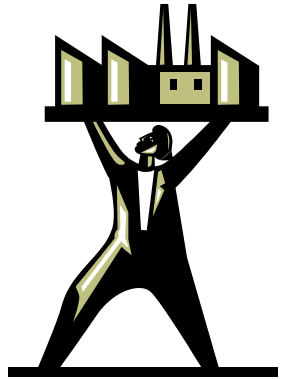
d. Control of the above

GMP for SME

Quality System - Personnel

a. Adequate number of staff
b. Some staff defined
    a. Head of Production
    b. Head of Quality Assurance
    c. Qualified Person
c. Adequately trained staff
d. Staff retention / loss of knowledge

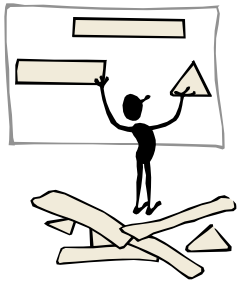




GMP for SME

Quality System – Key Components

i. Management of change



ii. Management of deviations / non conformances

iii. Management of complaints

Supply Chain Management

- Contracts – detailed guidance in chapter 7
- Supplier approval - audits?
- Testing of deliveries – batch acceptance
- Resilience of the supply
  - approve a number of suppliers for critical materials
  - Risk assess the supply chain
  - Assess impact of a change on product / comparability

Investigational Medicinal Products and Clinical Trials

Key legislative references

- Dedicate Annex in the guidelines – Annex 13
  - Manufacture according to GMP
  - Release of batches by QP –batch certification defined
  - http://ec.europa.eu/health/files/eudralex/vol-4/2009_06_annex13.pdf
- EMA Clinical Trials information
  - http://www.ema.europa.eu/ema/index.jsp?curl=pages/special_topics/general/general_content_000489.jsp&mid=WC0b01ac058060676f
  - http://ec.europa.eu/health/human-use/clinical-trials/index_en.htm

The Qualified Person

- Legislative reference is article 48 of Directive 2001/83/EC with responsibilities defined in article 51
- Guideline is Annex 16 (new draft in the progress)
  - Batch testing and release of products manufactured in EC/EEA;
  - Batch testing and release of products imported from a third country;
  - Release of products imported from a third country (MRA partner);
  - Routine Duties of the QP section 8

Take Home

- Guidelines are available
  - Can we interpret
  - Specialist knowledge required
  - QP
- Early contact essential
  - Transition from lab to putting a product into a human / animal

Take Home

- Advice – (medicinal product Competent authority)
- Contact should be on-going
- Takes time from application to award of a manufacturing/ importation authorisation

Thank you for your attention!