Normas de correta fabricação de APIs e Produtos Manufaturados.
Experiência da Industria Farmacêutica Europeia.

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ASSOCIAÇÃO PORTUGUESA DE MEDICAMENTOS GENÉRICOS E BIOSSIMILARES

Good Manufacturing Practice

1) Definition

2) GMP Guidelines

3) Working in a GMP environment

4) History and applicable legislation in EU

5) Major obstacles of recent EU Legislation related to GMP

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1 – Definition

- Good Manufacturing Practice (GMP) is a system for ensuring that products are consistently produced and controlled according to quality standards. It is designed to minimize the risks involved in any pharmaceutical production that cannot be eliminated through testing the final product.
- GMP covers all aspects of production from the starting materials, premises, and equipment to the training and personal hygiene of staff. Detailed, written procedures are essential for each process that could affect the quality of the finished product. There must be systems to provide documented proof that correct procedures are consistently followed at each step in the manufacturing process - every time a product is made

2 – GMP Guidelines

- EU GMP Guidelines
- WHO Good Manufacturing Practices
- Canadian GMP Regulation
- Australian GMP Regulation
- US GMP Regulation
- China GMP Regulation
- Brazil GMP Regulation

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3 - Working in a GMP Environment

- Most GMP requirements are very general and open-ended, allowing each manufacturer to decide individually how to best implement the necessary controls.

Positive aspect: allows flexibility and implementation according to business reality

Less positive aspect: GMP Guidance is not harmonized in all countries and regions , making it difficult for manufacturers to comply with requirements of all inspecting bodies.

4 - History and Applicable Legislation in EU

- History

First Edition was published in 1989

Second Edition was published in 1992, already including 12 Annexes

Re-structuring of GMP Guidance in 2005, consisting of Part I for Medicinal Products and Part II for Active Substances acting as Starting Materials, including 19 annexes

4 - History and Applicable Legislation in EU

Applicable Legislation

- **Commission Directive 2003/94/EC, of 8 October 2003, laying down the principles and guidelines of good manufacturing practice in respect of medicinal products for human use and investigational medicinal products for human use.**

- **Commission Directive 91/412/EEC of 23 July 1991 laying down the principles and guidelines of good manufacturing practice for veterinary medicinal products.**

- **Commission Delegated Regulation (EU) 2017/1569 of 23 May 2017 supplementing Regulation (EU) 536/2014 of the European Parliament and of the Council by specifying principles and guidelines for good manufacturing practice for investigational medicinal products for human use and arrangements for inspections**

- **Commission Directive (EU) 2017/1572 of 15 September 2017 supplementing Directive 2001/83/EC of the European Parliament and of the Council as regards the principles and guidelines of good manufacturing practice for medicinal products for human use**

4 - History and Applicable Legislation in EU

- Guidelines

Eudralex – Volume 4

Part I - Basic Requirements for Medicinal Products (9 Chapters)

Part II - Basic Requirements for Active Substances Used as Staring Materials

Part III – GMP Related Documents (8 documents)

Part IV – Annexes (19)

5 - Major obstacles of recent EU Legislation related to GMP

- Related to GMP for Active Pharmaceutical Ingredients and the enter into force of the Falsified Medicines Legislation: mandatory audits of API manufacturers by Finished Product Manufacturers:

1 - heavy workload and very expensive for both parties

2 – different outcomes from between auditors and between auditors and authorities

5 - Major obstacles of recent EU Legislation related to GMP

- Related to Finished Product Manufacturers (FPMs) qualification as suppliers through in situ audits:

FPMs are permanently being audited by different clients with different requirements

6- GMP certification for Finished Product Manufacturers

- The objective of a FPM is to be certified by the biggest number of authorities worldwide in order to produce for several countries
- The implication is being inspected by several inspecting authorities with different criteria, since countries do not recognize the GMP standards of each other
- Some authorities are not easily available to perform inspections

6- GMP certification for Finished Product Manufacturers

- What can be done?

PIC and PIC/S

PIC was established in 1970 and was extended to PIC/S (Pharmaceutical Inspection Co-operation Scheme) in 1995. Countries that are PIC members and have MRA recognize each other GMP certifications (Australia, Canada, Israel, Japan, New Zealand, Switzerland, United States)

7 - Conclusion

- Application of GMP Guideline: what does it mean?

- Several basic and common worldwide principles and requirements that aim to assure that finished product formulation and active ingredients are consistently high in quality, from batch to batch, for their intended use.

But also

- Several local requirements and different interpretation

Good Manufacturing Practice

- Thank you