GMP more than 3 letters

Point of view of an authority

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Conflicts of interest:

Relevant Financial Relationship

NONE

Off-Label Investigational Rules

NONE

Question : yes or no ?

1) Can a facility comming from an hospital envirronement become GMP ?

2) QP is not mandatory if a hospital pharmacist is incuded in the staff ?

3) Sterility is well known in hospital , so that’s not a real issue for a site in an hospital ….

A word bout my organisation

famhp
federal agency for medicines and health products

We are the national competent authority for ıes and Health Products in Belgium

We are competent for:

- Human and vet medicinal products : products and operators authorisations, all inspections or controls in relation .
- MD : NB surveillance, registration and inspections of actors and market surveillance.
- Human body materials : blood , cells including reproductive cells.

But not for:

- organ transplantations
- GLP
- cosmetics
- food complements …..

A word about me.

-) Pharmacist

-) Experiences :

- biological analysis
- public pharmacy
- GDP operator
- teacher for technical assistants
- worker at the Belgian pharmacoea commision
- GMDP inspector
- JAP auditor

-) Today : head of industry division

➔ Coordination of GMDP and GCP inspections and related matters : RAS , QP registration , post-marketing sampling plan.

-) During Covid pandemia :

-) Coordination of homecare oxygenotherapy

G. M. P. What is it ?

Good manufacturing practices can be regarded as a (very very very long) list of „ technical advices", recommandations, explanations, obligations …..

But basicaly it's a

➔ **quality assurance system .**

➔ adaptable, scalable, on the move …..

A never ending story !

G. M. P. What is it ?

Today I will speak only about :

GMP from Eudralex Vol 4 for medicinal products

G. M. P. What is it ?

AS GMP GMP like GMP light ➔ BAD WORDS

If you want to take principles from the text ➔ **write an adapted text :**

VOL 4:

-) GMP II

-) ATMP stand alone

NATIONAL:

-) Vet autovaccines (FR , UK)

-) Compounding unit (BE)

-) Special manufacturer (UK)

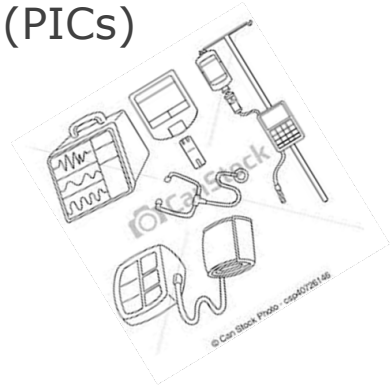
INTERNATIONAL

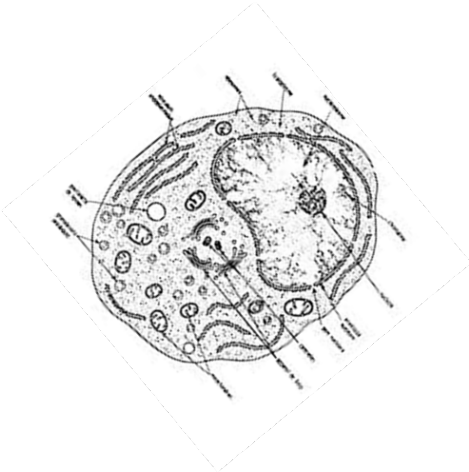
-) Preparation in health care institution (PICs)

PRINCIPLES WITH OTHERS TEXTS :

-) Human Body Materials

-) Medical devices





G. M. P. For what ?

For what kind of products ?

It's the same words for many thinks :

- Cosmetics
- Food
- Food complements
- ….

Are they the same texts / same requirements ?

NO but they are all quality systems

G. M. P. What is it **not** ?

Be carrefull

A miracle, a magic potion ➔ let's work and think my friends !

An HSA rule or an environmental guide : GMP protect the MP from the environement but not the environment from the product or the manufacturing process.

A ISO / CEN normes : taken in count but not the same terminology.

An absolute and unbreakable rule:

the guide is adapted regularly

measures can be equivalent to … but validated

A 100 % assurance : you have to take in count a GOOD risk analysis

G. M. P. Where are they applicable?

Everywhere ..... but .....

You can found:

EU GMP guide

FDA GMP guide

ASIAN GMP guide

WHO GMP guide

PICs GMP guide

SAME RULES (99%) but the devil is in the little things .

More a issue for big pharma .

G.M.P. in Eudralex

Part I - Basic Requirements for Medicinal Products

- Chapter 1 - Pharmaceutical Quality System (into operation since 31 January 2013)
- Chapter 2 - Personnel (into operation since 16 February 2014)
- Chapter 3 - Premise and Equipment (into operation since 1 March 2015)
  - See transitional arrangement for toxicological evaluation on page 1 of Chapter 3
  - Previous version
- Chapter 4 - Documentation (January 2011)
- Chapter 5 - Production (into operation since 1 March 2015)
  - See transitional arrangement for toxicological evaluation on pages 1-2 of Chapter 5
  - Previous version
- Chapter 6 - Quality Control (into operation since 1 October 2014)
- Chapter 7 - Outsourced activities (into operation since 31 January 2013)
- Chapter 8 - Complaints and Product Recall (into operation since 1 March 2015)
- Chapter 9 - Self Inspection

Part II - Basic Requirements for Active Substances used as Starting Materials

- Basic requirements for active substances used as starting materials (August 2014)

G.M.P. in Eudralex

Part III - GMP related documents

- Site Master File
- Q9 Quality Risk Management
- Q10 Note for Guidance on Pharmaceutical Quality System
- MRA Batch Certificate
- Template for the "written confirmation" for active substances exported to the European Union for medicinal products for human use (Version 2, January 2013)
- Guideline on setting health based exposure limits for use in risk identification in the manufacture of different medicinal products in shared facilities
- Guidelines of 19 March 2015 on the formalised risk assessment for ascertaining the appropriate good manufacturing practice for excipients of medicinal products for human use (all language versions are available here). A risk assessment as set out in these guidelines should be carried out for excipients for authorised medicinal products for human use by 21 March 2016.
- Template for IMP batch release (applicable as from the date of entry into application of Regulation (EU) No 536/2014 on Clinical Trials)

G.M.P. in Eudralex

ANNEXES

1. **STERILE PRODUCTS**
2. BIOLOGICAL (DS and DP)
3. **RADIOPHARMACEUTICALS**
4. VET PRODUCTS
5. IMMUNOLOGICAL VET PRODUCTS
6. MEDICINAL GAZES
7. HERBAL
8. SAMPLING STARTING AND PACKAGING MATERIALS
9. LIQUIDS, CREAL AND OINTMENTS
10. ..PRESSURED METERED DOSE AEROSOLS FOR INHALATION
11. COMPUTERISES SYSTEM
12. USE OF IONISING RADIATION INMANUFACTURING
13. **IMP ➔ to be changed by CTR**
14. BLOOD AND PLASMA HUMAN DERIVATED PRODUCTS
15. **QUALIFICATION AND VALIDATION**
16. **CERTIFICATON AND BR**
17. PARAMETRIC RELEASE
18. REFERENCE AND RETENTION SAMPLES

GMP in Eudralex

Glossary

- Glossary

Part IV - GMP requirements for Advanced Therapy Medicinal Products

- Guidelines on Good Manufacturing Practice specific to Advanced Therapy Medicinal Products

Other documents related to GMP

- Compilation of Community Procedures on Inspections and Exchange of Information updated to include new EU formats and procedures
- A revised version of the "Guidelines on Good Distribution Practice of Medicinal Products for Human Use" was published in the Official Journal and is applicable as of 24 November 2013 (OJ C 343/1, 23.11.2013).
- Guidelines of 19 March 2015 on principles of Good Distribution Practice of active substances for medicinal products for human use (all language versions are available here). These guidelines will come into operation on 21 September 2015.

GMP „on a nut shell“
or all the rules in **10 GOLDEN RULES**

#1: Get the facility design right form the start

#2: Validate your process and take count of the change control concept

#3: Write good procedures and follow them

#4: Identify who does what, determine responsability, don‘t have gap

#5: Keep good records : if it‘s not written down then it didn‘t happent!

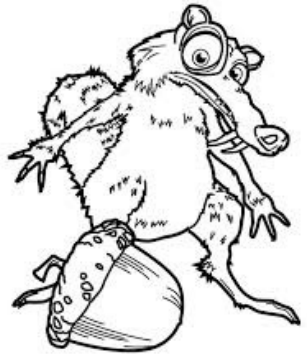
#6: Train and develop staff

#7: Practice good hygine

#8: Maintain facilities and equipment

#9: Design qualty in all the product lifecycle

#10: Perform regular audit : internal , external and ……inspections



Is it difficult to be / to become G.M.P. ?

YES and NO :

You must have :

-) a decision
-) a goal
-) a project leader
-) be open minded
-) never say « we do like this for years «
-) time more than money
-) a good pen ….
-) go outside to see people working
-) be audited
-) be inspected
-) write a CAPA plan
-) correct it
-) implement it …. tomorrow and after
-) be re audited , re inspected

➔ PLAN , DO, ACT, CHECK …

Is it true ?

!!!!!!!!!!!!!!!!!!!!!! YES WE CAN !!!!!!!!!!!!!!!!!!!!!!

Coming from an hospital environment can we become a GMP site ?

For all type of products?

As rapidly as commercial sites ?

What are the more frequent deficiences ?

Are they the same than in industrial envirronment ?

Is it true ?

Some figures :

8 years

13 sites : 60 % ATMP , 15 % Radiopharm and 25 % Classical

26 inspections

Excluded :

Sites with a commercial partnership
Sites as soon as they move out of the hospital (spin off)

Is it true ?

Coming from an hospital environment can we become a GMP site ?

YES for 40%

For all type of products?

ATMP : 30 % Radioph :100 % 66 % Classical Forms

Why not ?

Multifactorial

ATMP : **status of the product , become a spin off,** negative advice…

Classical : abandonment of the project….

Is it the same in commercial environment ?

No: more or minus 10 % of final negative advice.

Completion time ?

Much longer. **3 times**

In hospital environment : average of 9 month between the first visit and te first positive advice ; in the commercial one : < 3 month .

Is it true ?

!!!!!!!!!!!!!!!!!!!!!!!!!!   YES WE CAN   !!!!!!!!!!!!!!!!!!!!!!

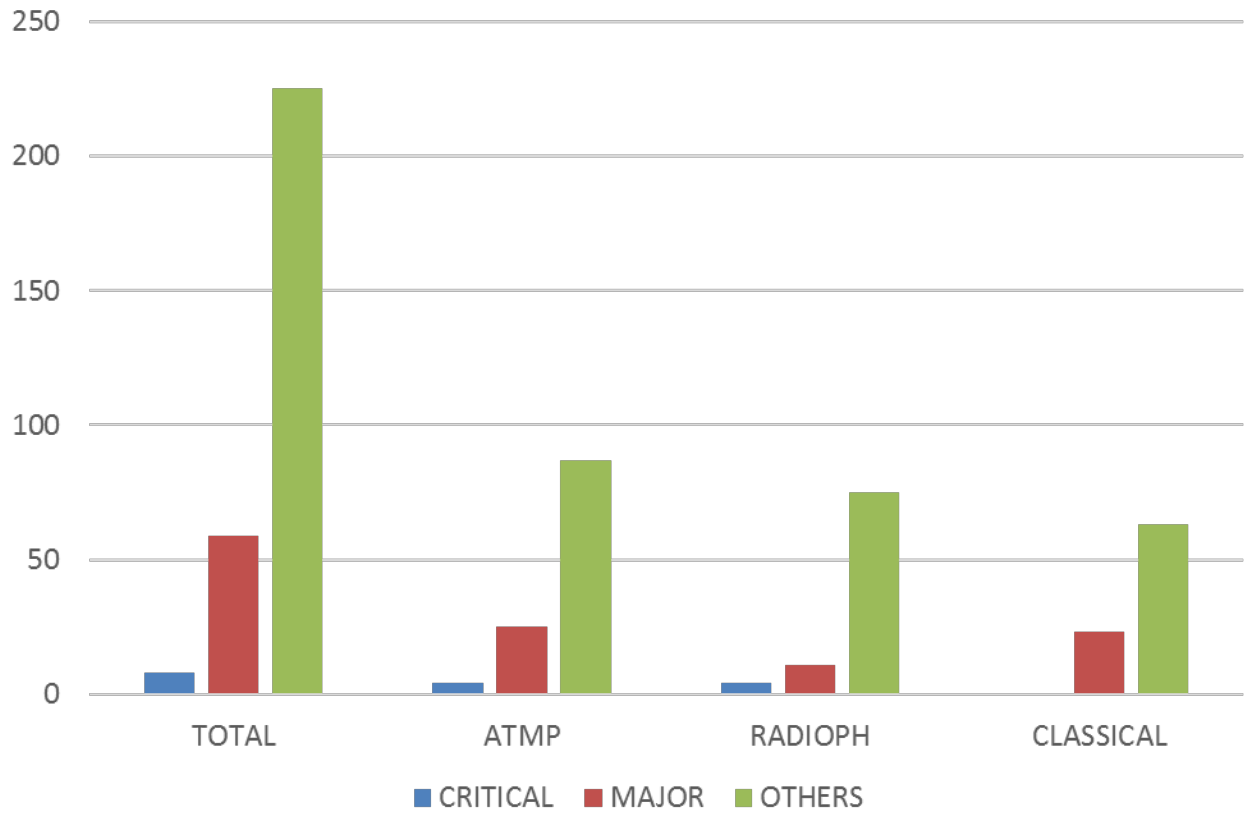
How many deficiences ?

Which type ?

What are the more frequent deficiences ?

Are they the same than in industrial envirronment ?

Number of deficiences



Critical deficiency

- **Definition from Compilation of Community Procedures :**

✓ A critical GMP failure occurs when a practice could give rise to a product which could or would be harmful to the patient, or which has produced a harmful product.

- **Consequences:**

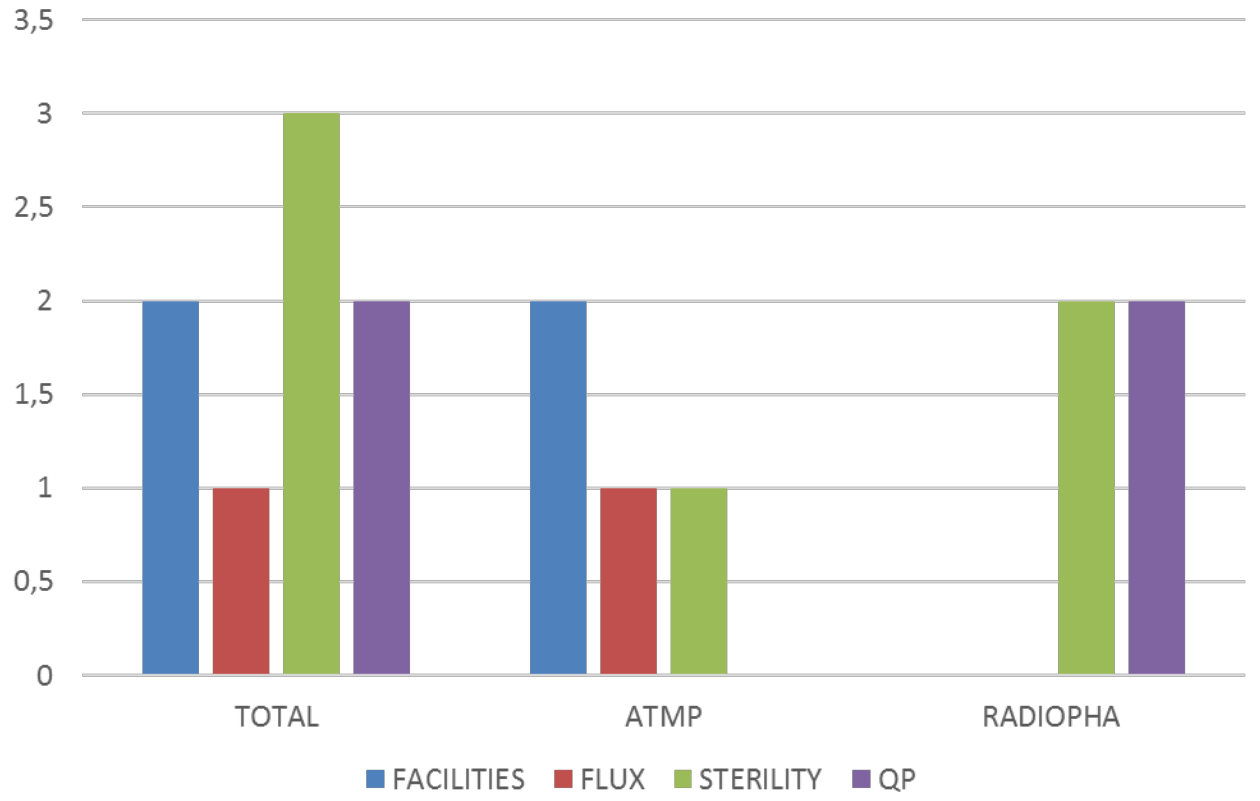
✓ Immediate action: recall, stop production

✓ Possible withdrawed cert GMP on Eudra GMP, …

✓ Capa

✓ Follow up inspection

WHICH TYPE OF CRITICAL



TOP 3 critical for commercial sites

- Building and equipment
- Documentation ➔ not the same
- Annex 1/ Sterility

Stats 2016 , not the same classification,

Major Deficiency

- **Definition from CCP:**

✓ A non-critical deficiency which has produced or may produce a product, which does not comply with its MA;

✓ *Or a* non-critical deficiency which indicates a major deviation fromGMP; a major deviation from the terms of the MA;

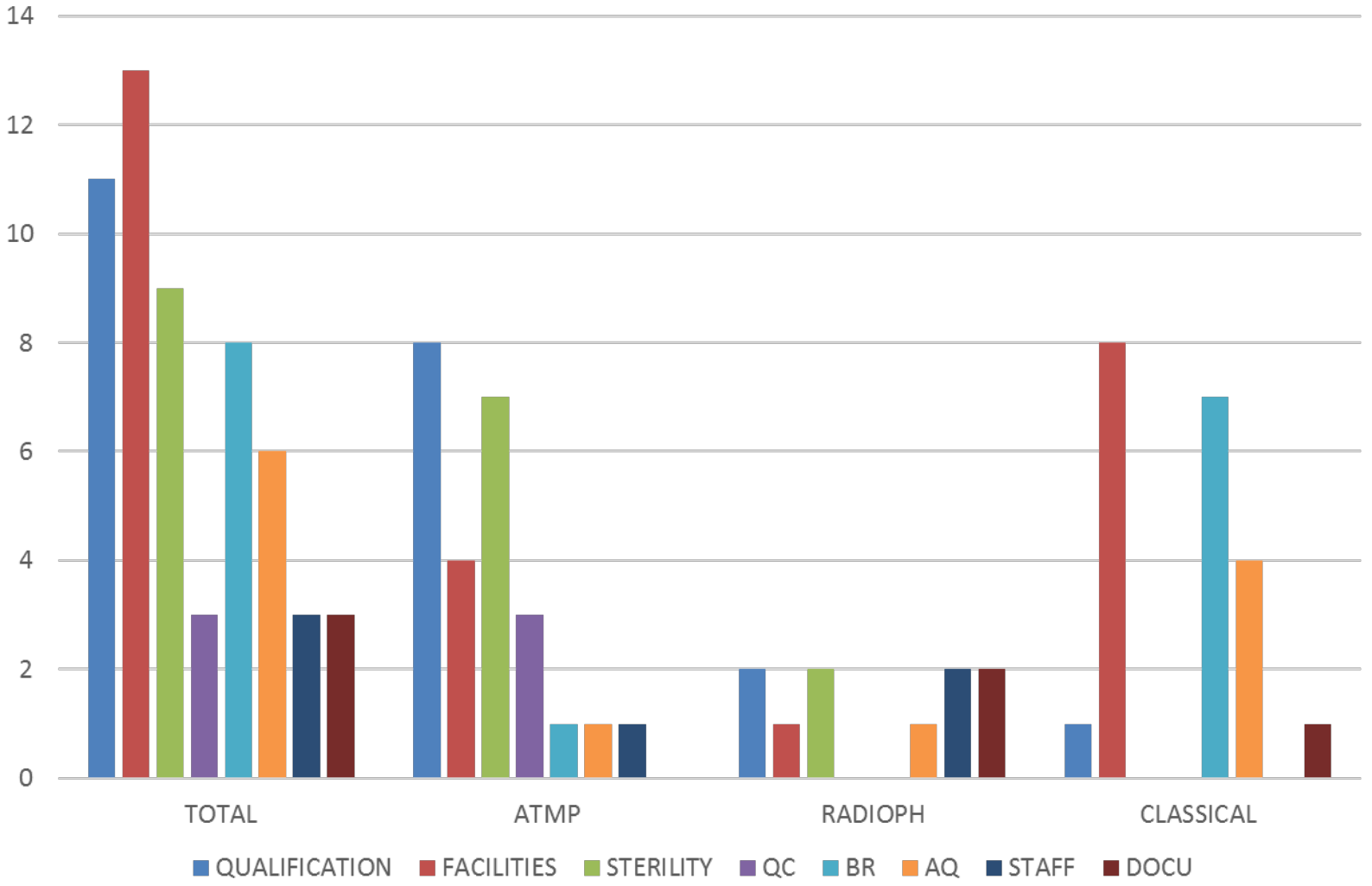
✓ *Or a* non-critical deficiency which indicates a failure to carry out satisfactory procedures for release of batches

✓ or a failure of the Qualified Person to fulfill his legal duties;

- **Consequences:**

✓ CAPA, imposed deadlines
✓ Recall

WHICH TYPE OF MAJOR ?



TOP 3 major for commercial sites

- Building and equipment
- Production ➔ not the same
- Documentation

3 take home messages

- GMP is more a lind set than a long boring text.
- It’s possible to respect GMP in a small scale site.
- Radiopharmaceutical products can be GMP in an hospital.

Thank you for your attention and stay safe !

Contact

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