EXPERT
SANTÉ CANADA
MAPAQ

Maintenance

of Quality Control Laboratory equipment

PBE Expert Inc – CANADA

Training Company Agreement CPMT #0059104

Qualified MAPAQ Consultant

at the messure 2 of the Levier program

PBE, Training Company Agreement **CPMT** #0059104

Commission des partenaires du marché du travail
Québec

CERTIFICAT D'AGRÉMENT

Loi favorisant le développement et la reconnaissance des compétences de la main-d'oeuvre

Titulaire : PBE, PHARMA BIO EXPERT INC.

Numéro d'agrément : 0059104

NEQ : 1168916956

Catégorie d'agrément : Organisme formateur

Date de délivrance : 6 février 2018
Date d'échéance : 5 février 2020

CHAMPS PROFESSIONNELS

01 Administration et commerce
03 Alimentation, hôtellerie et tourisme
06 Chimie et biologie

Par : Isabelle Bergeur

Le 7 février 2018

La délivrance du certificat est valide en fonction des documents soumis à la Commission des partenaires du marché du travail.

Ministère du Travail, de l'Emploi et de la Solidarité sociale

EQ-6282 (06-2003)
ENT-0031 (12-2016)

Summary

Regulatory framework :

Regulatory Framework: (cGMP)

World Health Organization (WHO)

- http://www.who.int/medicines/areas/quality_safety/quality_assurance/production/en/index.html

EU - EMEA

- http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol4_en.htm

United States – FDA 21 CFRs

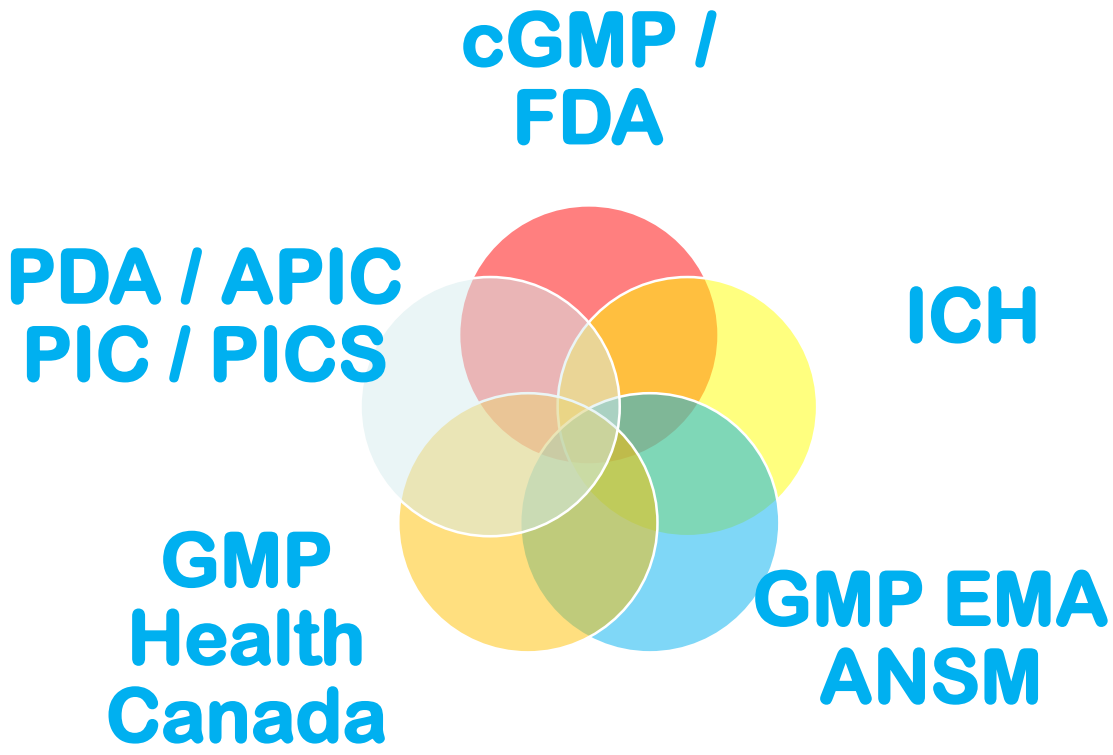
- http://www.fda.gov

Canada – Health Canada

- http://www.hc-sc.gc.ca/dhp-mps/compli-conform/gmp-bpf/index-eng.php
- ICH = International Conference on Harmonization

http://www.ich.org/products/guidelines/quality/quality-single/article/good-manufacturing-practice-guide-for-active-pharmaceutical-ingredients.html

Laws & regulations vs country ?



Normative requirements

- ✓ European Pharmacopoeia (Ph.Eur.)
- ✓ French Pharmacopoeia (Ph.F.)
- ✓ Pharmacopoeia Internationalis (Ph.I.)
- ✓ The British Pharmacopoeia (B.P.)
- ✓ The Canadian Formulary (C.F.)
- ✓ The National Formulary (N.F.)
- ✓ The Pharmaceutical Codex: Principles and Practices of Pharmaceuticals
- ✓ The United States Pharmacopoeia (U.S.P.)

Standards

- FDA CDRH Guidance for Sterilants & Disinfectants, 1/3/00.
- ICH Q7A, GMP for Pharmaceutical Active Ingredients.
- ICH Q3A : Impurities in New Drug Substances.
- ICH Q3B : Impurities in New Drug Product.
- ICH Q3C : Impurities, Residual Solvents.
- ISO/IEC 17025 : 2005.
- General requirements for the capability of calibration and testing laboratories.

Definition of a QCL

Definition of a QCL

QCL are subjected to the following standards:

- Good manufacturing practices (GMP).
- ISO 17025.
- Good Laboratory practices (GLP).
  - Standard operation procedures (SOP).
  - Qualified and trained staff.
  - Validation.
  - Documentation.

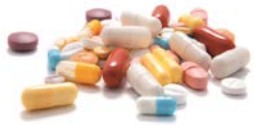
Definition of a QCL

- **Takes over the verification of the quality of the product.**
- **The following check-ups:**
  - Quality control of raw materials.
  - Quality control of packaging articles.
  - In-process quality control (IPC).
  - Finished products quality control.
  - Quality control of products during the quarantine period.
  - Quality control of clean utilities: PW, WFI, CCA, Gaz Pharma, etc.

Inspection of Quality Control Laboratories QCL

Quality Control Laboratories / QCL?

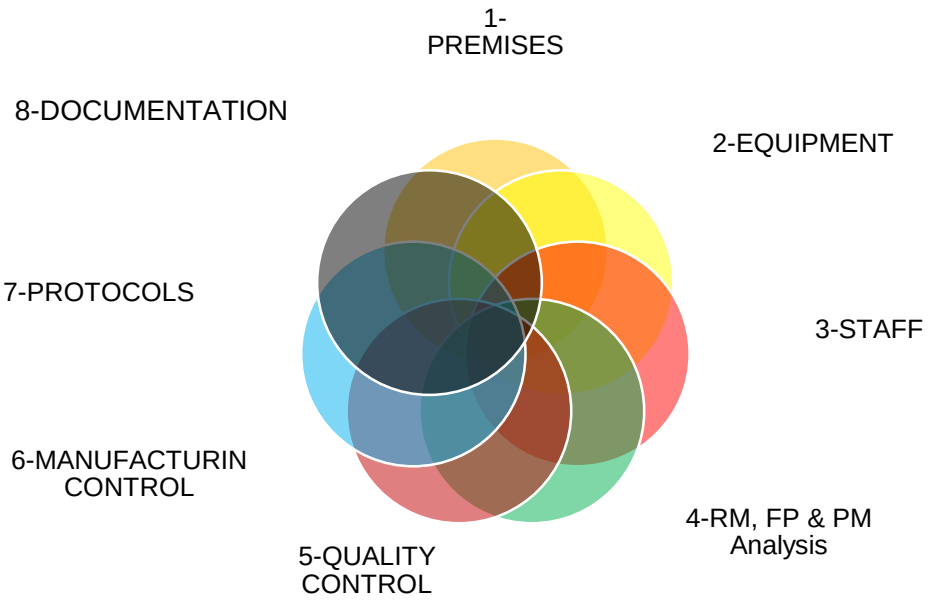
- Takes over the verification of the quality of the products.
- All these controls ensure a maximum level of quality of the drugs provided.



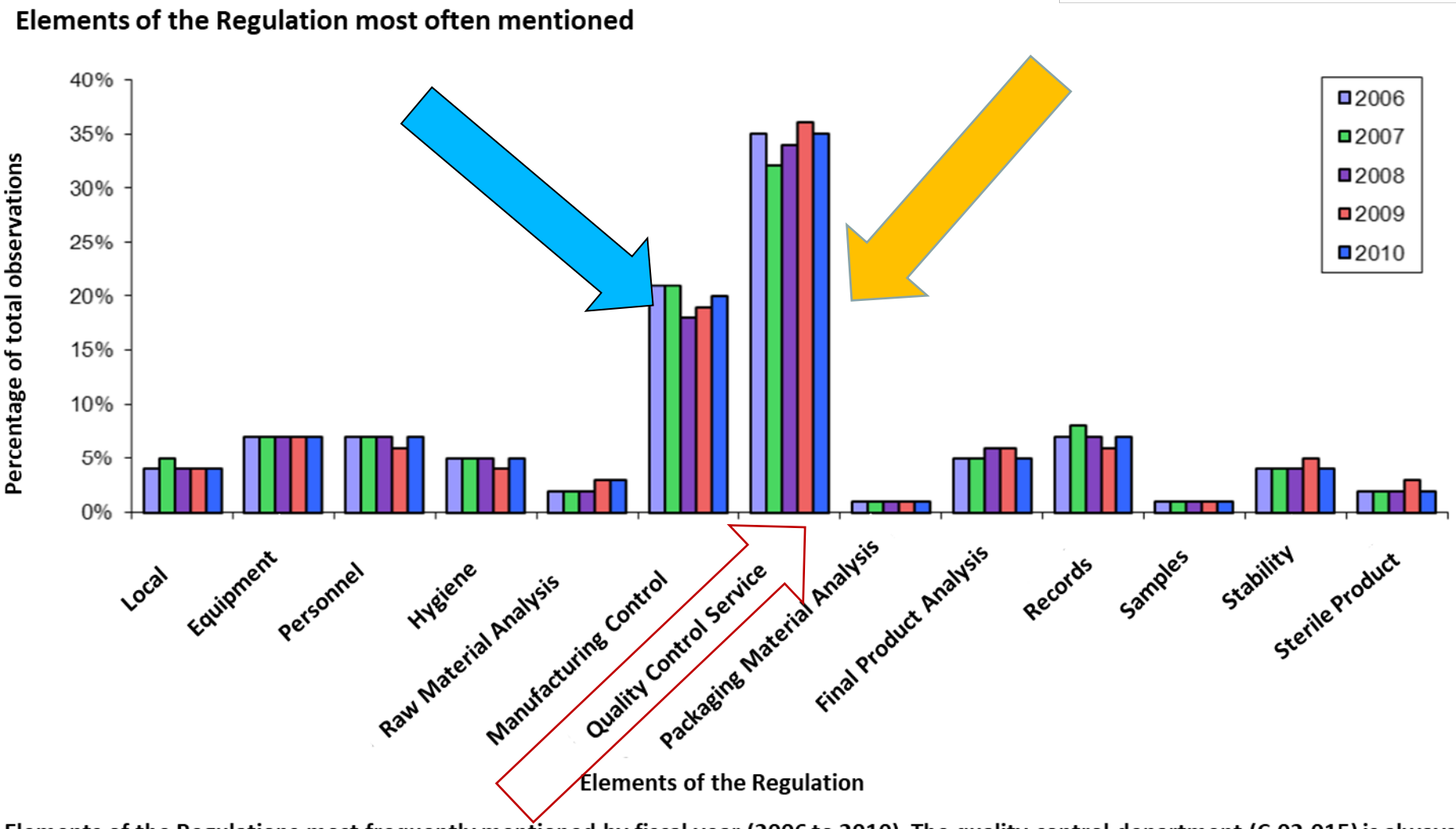
Quality control (continued)

Classifies the GMP/GLP production process in, at least, 8 categories:

1. Premises
2. Equipment
3. Staff
4. RM, FP & PM Analysis
5. Protocols
6. Quality control
7. Manufacturing control
8. Documentation / Records



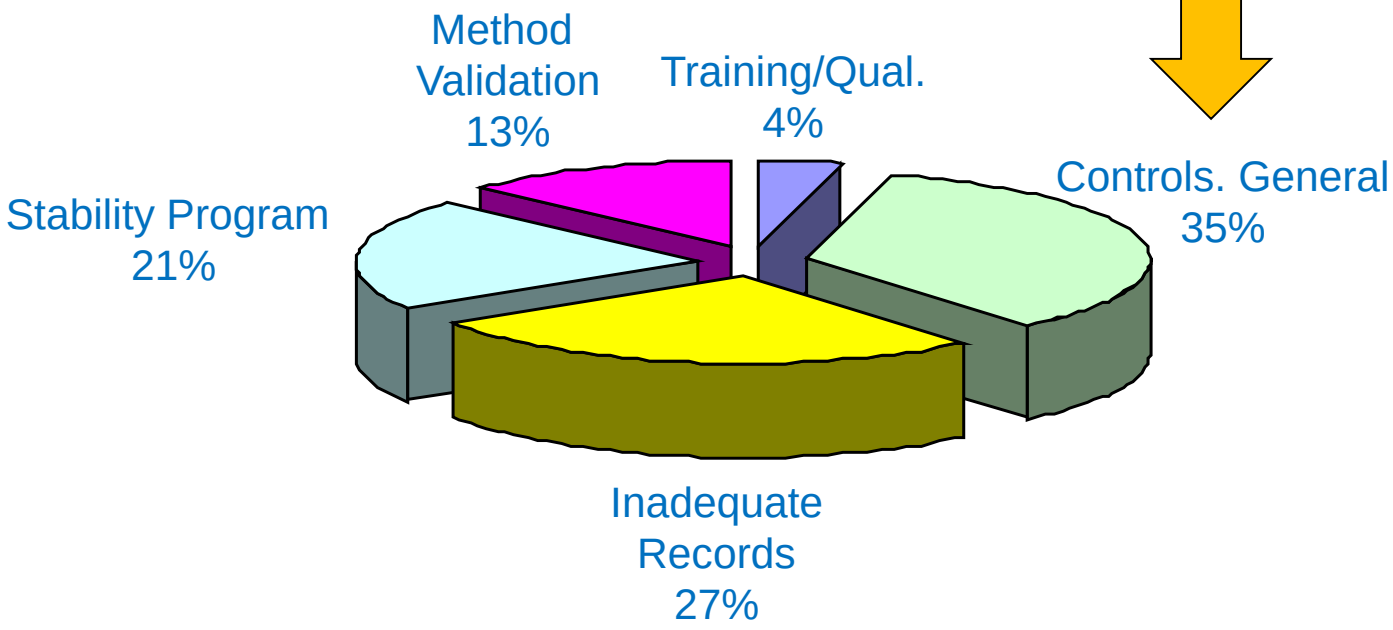
Importance of QCL?



Elements of the Regulations most frequently mentioned by fiscal year (2006 to 2010). The quality control department (C.02.015) is always the element with the greatest number of observations

FDA Systems Based Inspection: Laboratory System

Feb – July 2002: 212 Inspections (US)



* Reference: Albinus D' Sa, FDA, CDER Office of Compliance, from AAPS, Nov. 2002 presentation.

RAQP, WHY ?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Welcome to GlobalCompliancePanel's Live Webinar
Risk Analysis in Pharmaceutical Manufacturing: A Regulatory Overview
Tuesday, May 25, 2010
10:00 AM PDT | 01:00 PM EDT
By : Steven S. Kuwahara, Ph.D.
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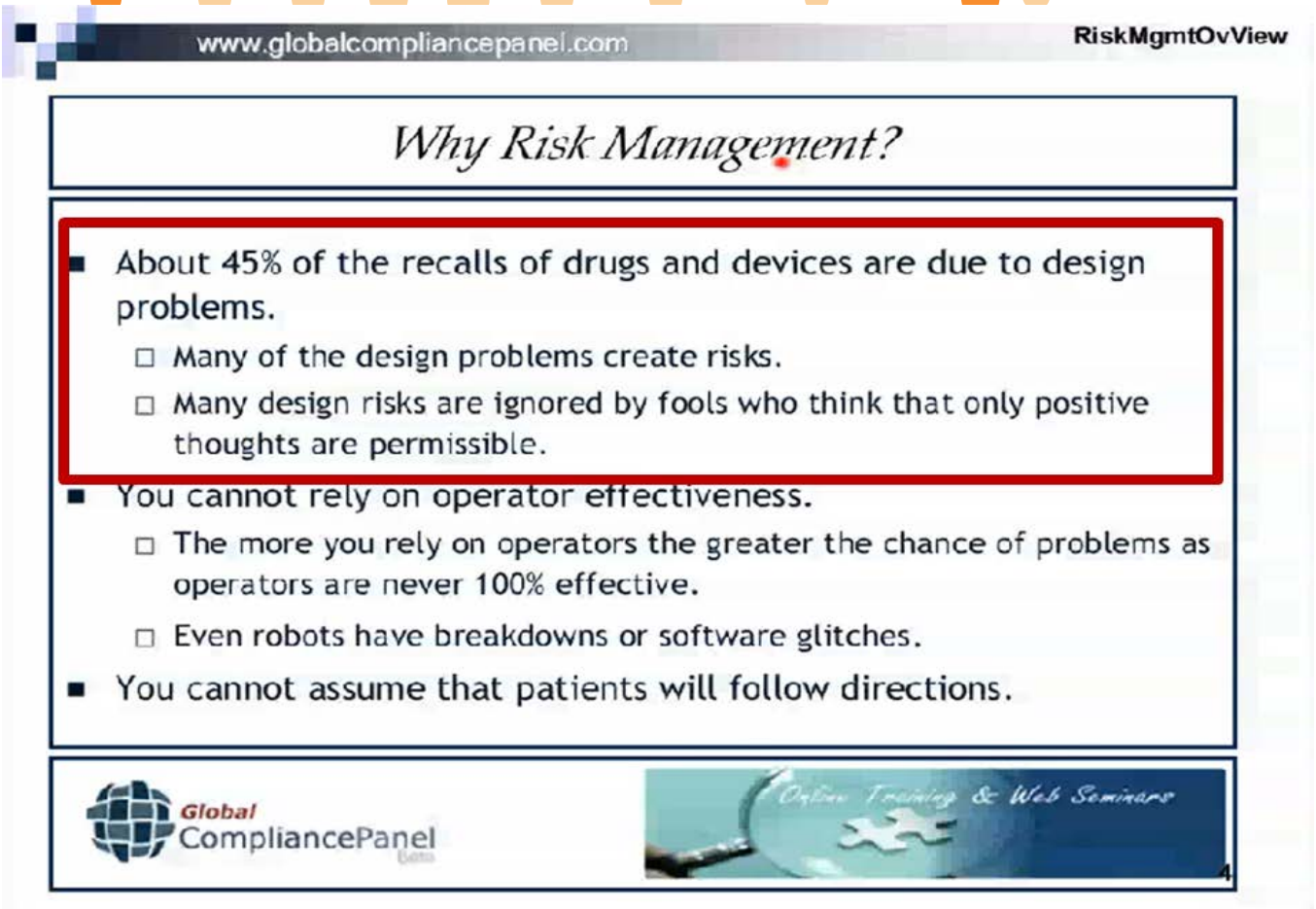
RAQP, WHY ?


www.globalcompliancepanel.com
RiskMgmtOvView
Why Risk Management?
About 45% of the recalls of drugs and devices are due to design problems.
Many of the design problems create risks.
Many design risks are ignored by fools who think that only positive thoughts are permissible.
You cannot rely on operator effectiveness.
The more you rely on operators the greater the chance of problems as operators are never 100% effective.
Even robots have breakdowns or software glitches.
You cannot assume that patients will follow directions.
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GLP vs glp

***Good Laboratory Practices*:**

- CFR 21, 58.
- Applies to pre-clinical studies
- Look up aspects that do not apply to quality control laboratories (pet shop, protocol, …).

good laboratory practices:

- Includes in GMPs and in *guidelines.*

FDA 483 observations on Product Quality

GMP /FDA Inspections:

- Several observations related to deficiencies in product quality reviews
- FDA 483 observations on Product Quality:
  - No procedures for product Quality reviews.
  - No conduct on product Quality reviews.
  - Various components of the reviews not carried out, insufficient investigations, no corrective actions or other conclusions.

CONTROL OF GENERICS BY THE AFSSAPS LABORATORIES

REVIEW OF THE CONTROL OF GENERICS BY THE AFSSAPS (1999 – 2006)

	REFERENCES		GENERICS		
	Number of specialties	Number of NC (% NC)	Number of specialties	Number of NC (% NC)	Statistical Test
Systematic checks (1999-2006)	314	19 (6,05 %)	1136	102 (8,98 %)	NS
Dissolution investigation (2001-2003)	17	0	30	3 (10 %)	NS
Motivated controls (2000-2006)	62	15 (24,19 %)	286	44 (15,38 %)	NS

CONTROL OF GENERICS BY THE AFSSAPS LABORATORIES

CAUSES OF NON-COMPLIANCE All types of programs combines	Princeps (N=393 sum of the 3 programs)	Generic Specialties (N=1452 sum of the 3 programs)
Active Principle Content	3 (0,8%)	20 (1,4%)
Cross-contamination	1*	
Galenic Tests (except breakability)	4	7
Breakability test	18 (4,6%)	68 (5,2%)
Organoleptic traits	3 (0,8%)	37 (2,5%)
Average mass/Uniformity of mass	3 (0,8%)	12 (0,8%)
pH		3
Dissolution tests		6
Presence of nonstandard impurities	2	4
Microbiological contamination	1	2
Labeling		2
1 specialty may have several types of non-conformities		

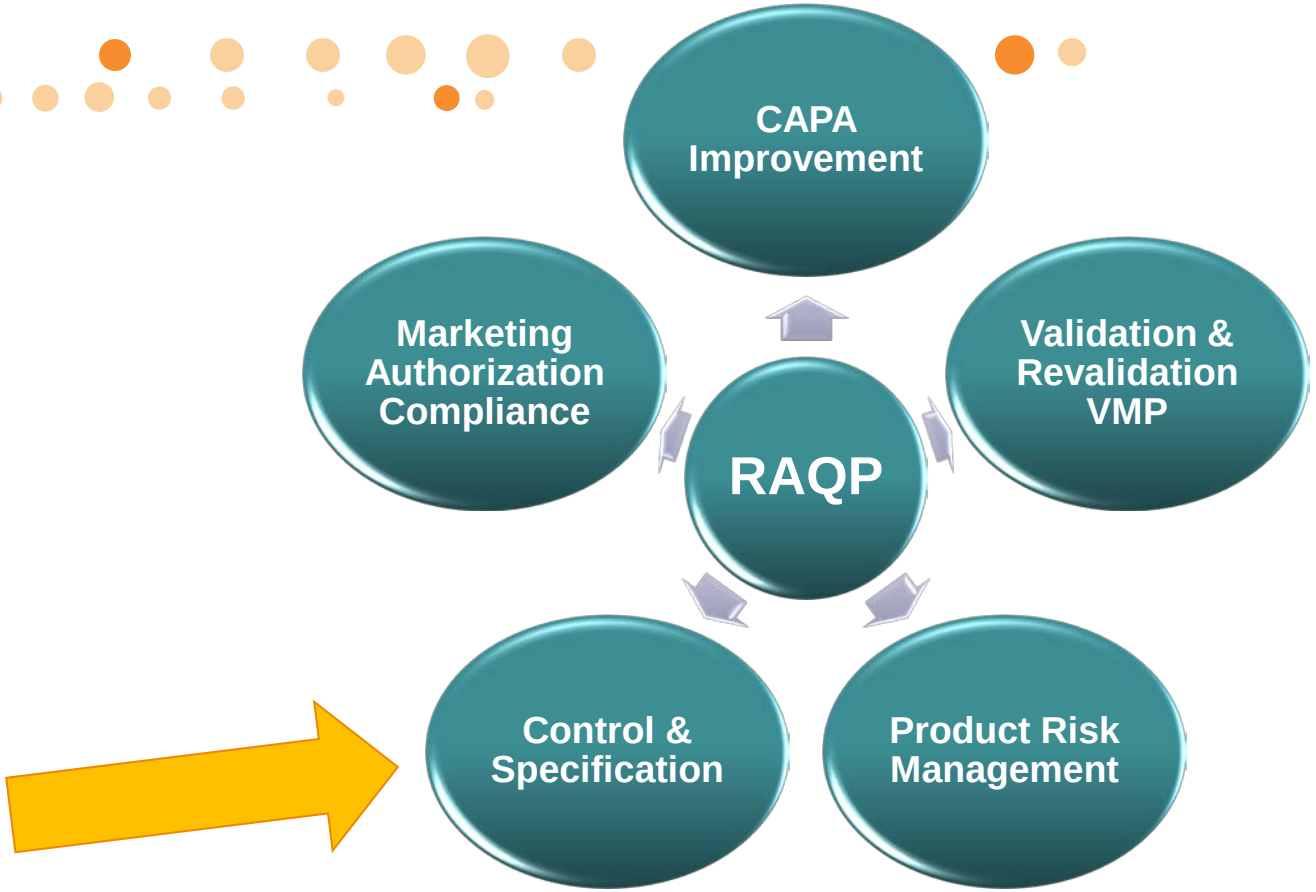
ACTIONS UNDERTAKEN BY THE AFSSAPS

Follow-up of inter-directional non-compliance meetings

Inspections	20
Batch withdrawals	11
Method/record/manufacturing changes	78
Re-checks, control of other batches/specialties	29
Modifications of processing	4
Modifications of formula	2
Manufacturing shutdowns	3
Foreign Inspection Information	3
In progress	17

167 Actions carried out for a total of 1845 specialties analyzed, on average 1 action for every 11 controlled products

QCL vs GMP


CAPA
Improvement
Marketing
Authorization
Compliance
Validation &
Revalidation
VMP
RAQP
Control &
Specification
Product Risk
Management

QCL vs GMP


Quality
Audit
Compliance
Batch
Disposal
External
Quality
Equipe
Qualité
Produit
Qc
API/PF
Product
Complaints
Investigations
Stability

QCL vs GMP

Manufacturing data

- Critical parameters – IPC product aspect

Packaging Data

- Yield
- RQP
- List of batches/periods

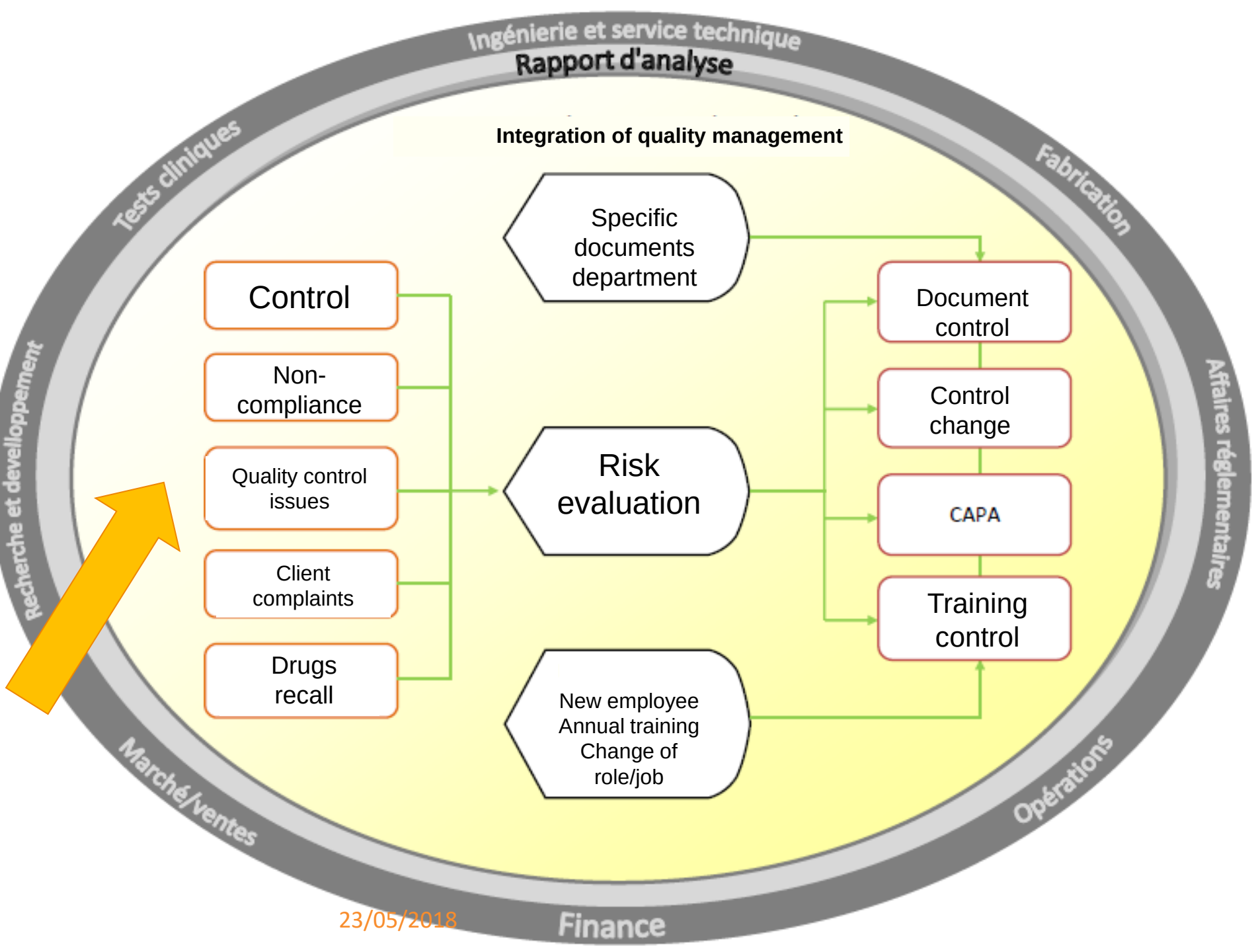
Quality Assurance Data

- Deviations
- Claims
- Recall
- Validation
- Qualification
- Control changes
- Providers

Control Laboratory Data

- Analytical results
- Sampling Aspects
- FUS stability

Supply Chain data


Ingénierie et service technique
Rapport d'analyse
Fabrication
Affaires réglementaires
Opérations
Finance
Marché/ventes
Recherche et developpement
Tests cliniques
Integration of quality management
Specific documents department
Control
Non-compliance
Quality control issues
Client complaints
Drugs recall
Risk evaluation
New employee
Annual training
Change of role/job
Document control
Control change
CAPA
Training control

QCL vs GMP

GMP – General Consideration:

1. Quality
2. Good manufacturing practices for pharmaceutical products (GMP)
3. Hygiene & ZAC
4. Qualification et validation
5. Complaints
6. Product recalls
7. Production in outsourcing contract analysis
8. Self-inspections & Quality Audits
9. Staff
10. Training
12. Quality control premises
13. Equipment
14. Materials
    - Reagents and growth medium
    - Reference standards
15. Documentation

QCL vs GMP

GMP – General considerations:

16. Good practices in quality control:

a. Control of raw materials, PM, and intermediate products, bulk and finished products.

b. Requirements of the analysis tests.

c. Review of batch records.

d. Stability studies.

GMP vs QCL – Management & Infrastructure

Inspection of QLCs / Priorities ? Vs Inspection QCL installations

- Staff et Direction
- Premises and equipment
- Procedures
- Calibration & preventive maintenance
- Raw data
- Standards
- Samples
- Documentation
- OOS
- Validation of equipment

Next generation maintenance techniques

Maintenance Policy

Types of maintenance

Levels of maintenance

Next generation maintenance techniques/ Levels of maintenance

- **Scale of "complexity" of maintenance actions.**

Lv.1
- Simple actions

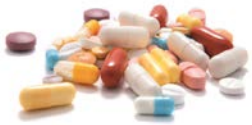
Lv.2
- Minor preventive operations maintenance

Lv.3
- Diagnosis required
- Specialized technician intervention

Lv.4
- Important corrective or preventive maintenance work

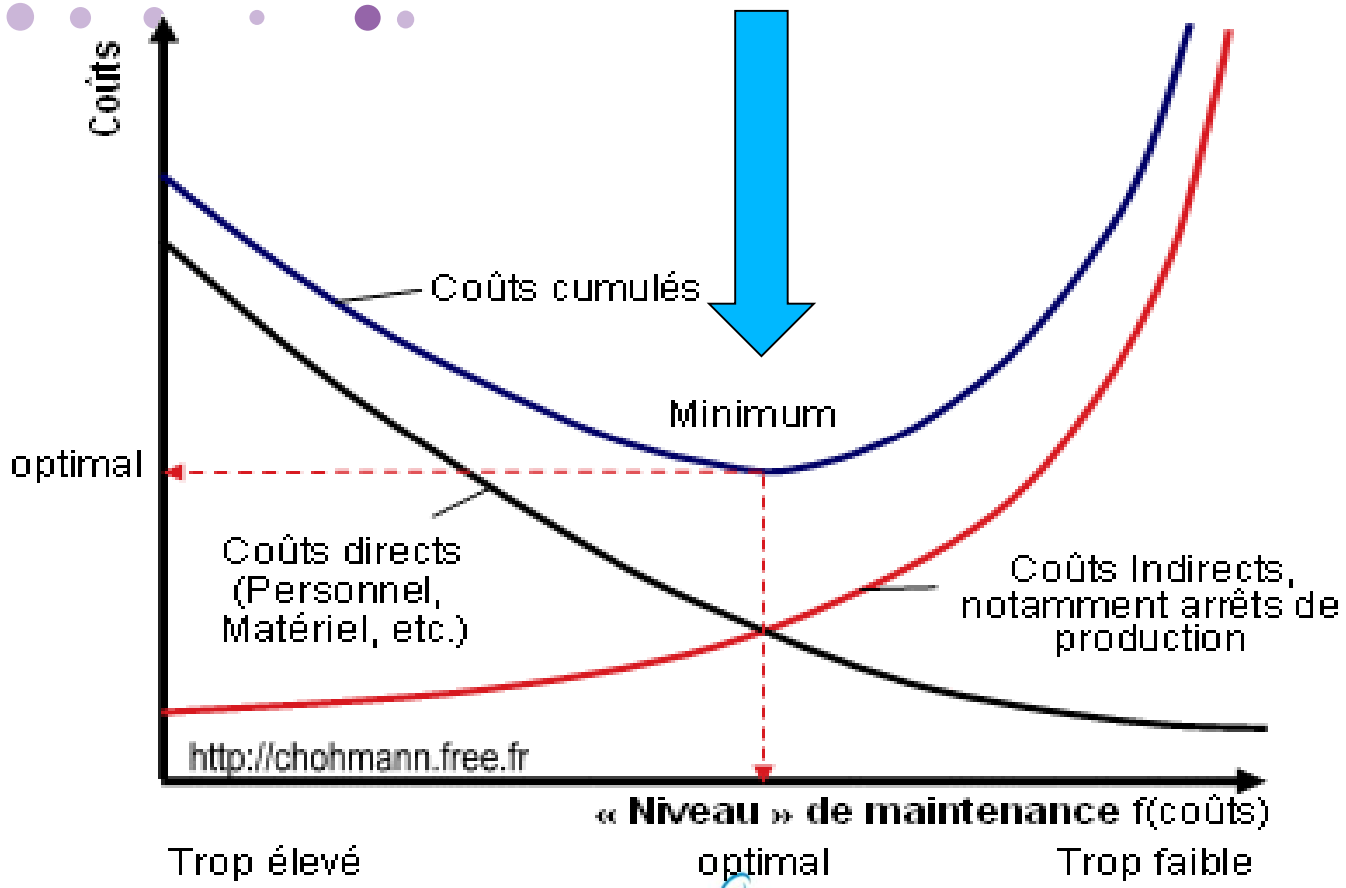
Lv.5
- Renovations, reconstruction requires contractors

-



Tools and maintenance methods

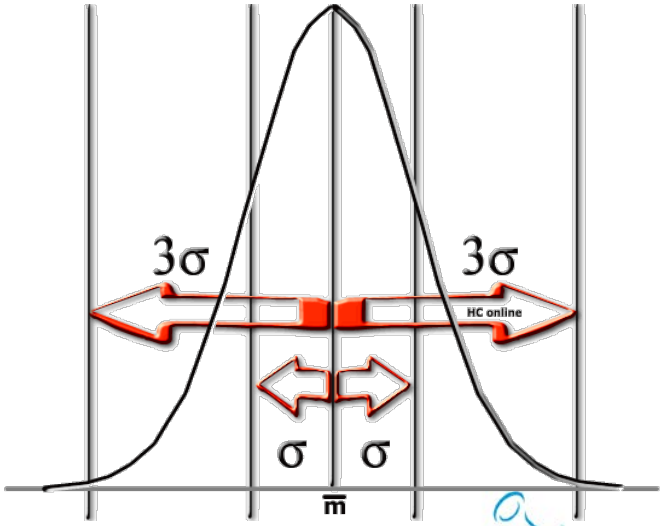
Next generation maintenance techniques/ Tools & maintenance methods - Lean Asset Management



Next generation maintenance techniques/ Tools & maintenance methods - 6 SIGMA

Six Sigma is a quality and profitability improving method based on statistical process control (SPC).

Six Sigma introduces a culture shift by seeking to reduce variability at all levels.

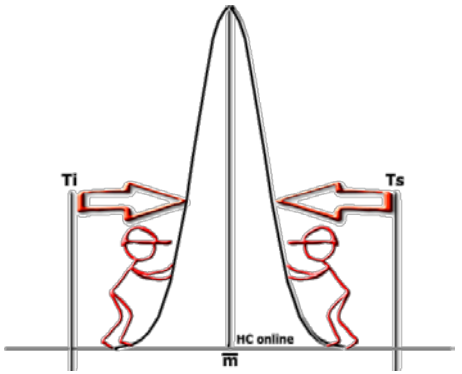


Next generation maintenance techniques/ Tools & maintenance methods - 6 SIGMA

Margin of error (6 Sigma) : 0.01 %

Source : José GRAMDI, UTT

±1σ	68,26%	31,74%
± 2σ	95,44%	4,56%
± 3σ	99,73%	2700ppm
± 4σ	99,994%	60ppm
± 5σ	99,998%	20ppm
± 6σ	99,9997%	3ppm



Goal: to reduce sigma

Next generation maintenance techniques / Tools and maintenance methods SMED

Next generation maintenance techniques/ Total Productive Maintenance (TPM)

Case Study 1 – TPM

Total Productive Maintenance / Context and prejudice

Case Study 1 – TPM

Total Productive Maintenance / 2- Real performance

Case Study 1 – TPM / Total Productive Maintenance / 3- TPM indicators

Case Study 1 – TPM / Total Productive Maintenance / 4- TPM ratios

Case Study 1 – TPM / Total Productive Maintenance / 5- TPM goals

Case Study 1 – TPM

Total Productive Maintenance / 6- The basics of TPM

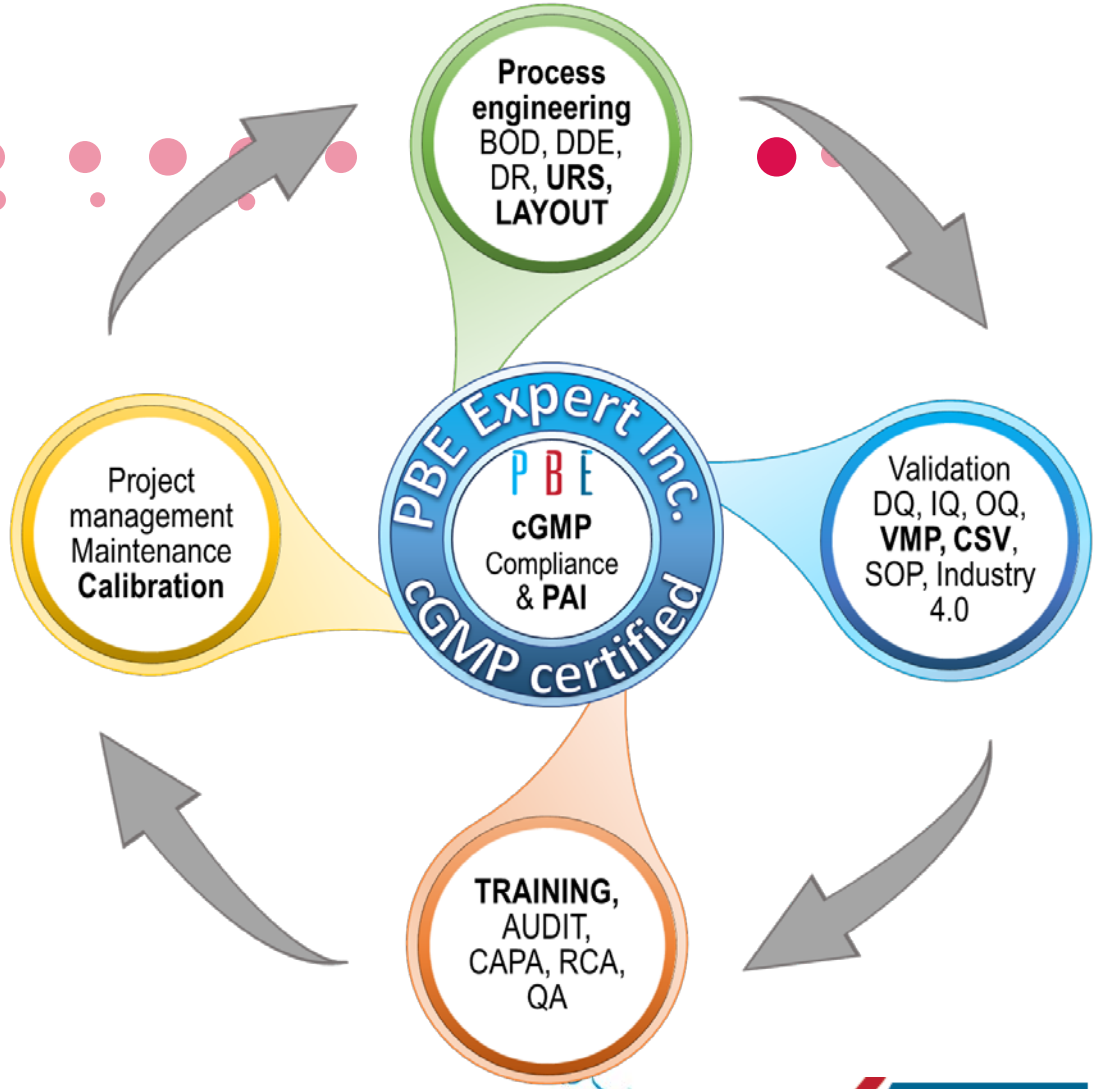
Case Study 1 – The 8 pillars of TPM

Next generation maintenance techniques/ Total Productive Maintenance- 8 pillars of TPM/ Management and autonomous maintenance

Management and autonomous maintenance of equipment:

1. Waste elimination/Improvement on a case by case basis.
2. Scheduled maintenance.
3. Improvement of knowledge and know-how.
4. Safety, working conditions and environment.
5. Proficiency in quality (maintenance).
6. Proficiency in product design and associated equipment.
7. Efficiency of related services or « TPM in the offices ».
8. Management and autonomous maintenance of equipment.

Quiz - Evaluation



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VURS
FURS
PURS
Product
Profit
Process
Partner
Performance
People
Project
Plant
8
11
1
13
1
25
20
21
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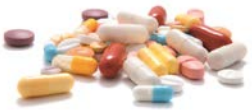

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