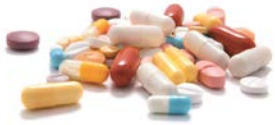


EXPERT
SANTÉ CANADA
MAPAQ

CLEAN IN PLACE
CIP
from sanitary design to validation

PBE-Expert Inc – CANADA

Training Company Agreement CPMT #0059104

Qualified MAPAQ Consultant

at the measure 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

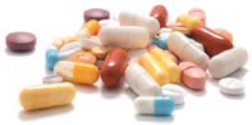
La délivrance du certificat est valide en fonction des documents soumis à la Commission des partenaires du marché du travail.

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

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

Goals of this training / CIP

1. Development of cleaning & disinfection processes.
2. Evaluation of selection criteria for cleaning & bio-decontamination agents (CDC).
3. Audit & prerequisites for cleaning validation.
4. Cleaning validation strategy.
5. Cleaning validation procedure.
6. List of potential contaminants.
7. Evaluation of critical time limits in a cleaning validation process.



Regulatory framework : Cleaning (cGMP)

Regulatory framework: Cleaning (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

Summary of regulatory requirements - EUROPEAN / www.dg3.eudra.org

Europeans : manufacturing, – GMP guides

- § 5.19 : « Use of cleaning procedures of known effectiveness»
- § 5.20 : « Measures taken to avoid cross-contamination as well as their effectiveness should be periodically monitored according to established procedures»
- Annexe 15 : Section 6 – Cleaning validation
- ANSM(AFSSAPS), LD.15. Cleaning validation p132
- PIC/S : Draft Annexe 15 of the GMP guide

www.picscheme.org

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.)

Development of cleaning processes

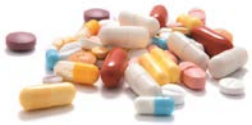
Summary: Cleaning & disinfection development processes in 10 points

1. What is a CIP ?
2. Benefits of a CIP ?
3. Why use a CIP ?
4. How does a CIP work ?
5. Details of a CIP
6. Type of CIP systems
7. CIP - SIP
8. Follow-up & Monitoring
9. Design considerations
10. Summary

PROBABLE CAUSES OF CIP MALFUNCTIONS? LOSS OF CONTROL OF CRITICAL PARAMETERS (CPP)

PROBABLE CAUSES OF CIP MALFUNCTIONS?

1. **Pump**, type, sanitary design, drain … ?
2. **Level in Tank**?
3. **Spray Balls**: technology, coverage, flow, diameter, pressure?
4. **Heat exchanger**? Health technology?
5. **Temperature range** (Alert/Alarm Limits) ?
6. **Control** of CPP ?
   a. Temperature,
   b. Time,
   c. Conductivity,
   d. Flow,
   e. Pressure.



2- Benefits of a CIP ?

TOP 10 CRITERIA of Sanitary Design

Benefits of CIP ?
TOP 10 CRITERIA of Sanitary Design

1. **Re**_____, Repeatable, **Va**_____, and Controlable Results.
2. Increased Productivity Through **Re**_____ in **Cleaning T**_____
3. Reduction of Chemical Products **Ha**_____ **(HSE).**
4. Increased **Pr**_____ considerations of Health and Safety / **HSE.**
5. Reduction of **En**_____ and legislative impacts.

I. Simple **Op**_____
II. **Ec**_____ of Costs of Utilities, Cleaning Agents and Effluents and Working Time, etc.
III. **Tra**_____ of Lots and Records.
IV. Reduced Cleaning **Ti**_____.
V. Possibility of utilizing **Higher Te**_____ **and** Stronger Chemicals Agents.

3. Why use a CIP ?

4. How does a CIP work?

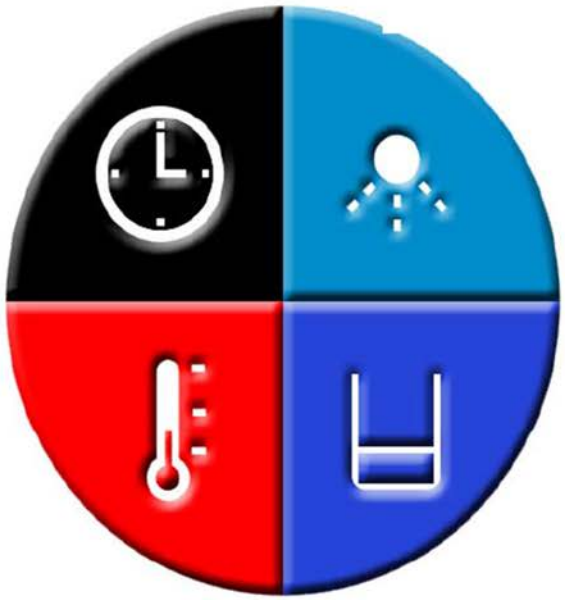
5. Details of a CIP

5. Details of a CIP

Source of Energy

Time

Mecanical

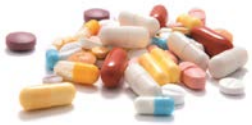


Temperature

Chemical

5. Details of a CIP

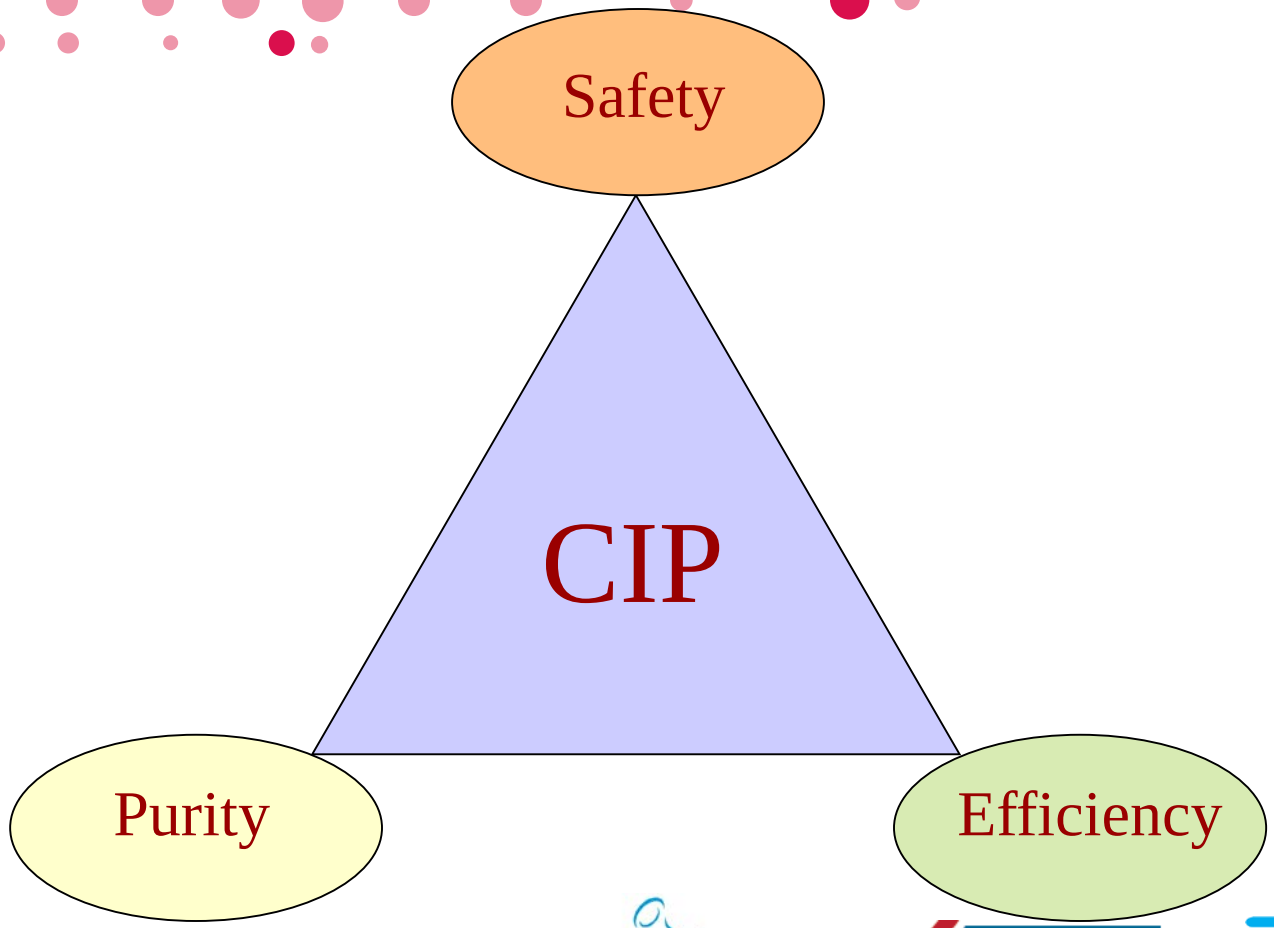
PARAMETER	MANUAL CLEANING	AUTOMATICAL CLEANING
TIME	Fast Latency between steps may vary	Higher Time Better Controlled Latency
FORCE	High force Difficult to quantify Non-uniform Difficult to reproduce	Low strength Difficult to quantify Uniform and reproducible VALIDATABLE
CONCENTRATION	Low: risk to the staff Low Toxic Detergent	More aggressive formulas -of risk for personnel
TEMPERATURE	Uncontrolled, variable SECURITY- - -	Much Higher, better controlled SECURITY +++



5. Details of CIP

Step	Operation	Cleaning Agent	Temperature (°C)	Time (mn)	Use
1	Pre-Rinse				
2	Alkali clean				
3	Inter-rinse				
4	Acid clean				
5	Inter-rinse				
6	Final Rinse				
7	Drying				
8	Disinfection (Optional)				

5. Details of a CIP



6. Types of CIP systems

6. Types of CIP systems

Two types of CIP:

1- Fixed CIP ?

2- Mobile CIP ?

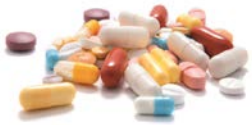
3- One tank?

4- Two tanks?

5- Three tanks?

Static CIP Unit

Typical Static CIP System



6. Comparison between various types of CIP systems

	Re-Use	Single Use
Number Cuves Solution	2 to 5	1 or none
Temperature of Solutions	Fixed	Ajustable
Concentration of Solutions	Fixed	Ajustable
Concurrency	Operation 1 to 4 (Multi-Channel)	Only 1
Flexibility	Low	High
Cross Contamination	High Risk	Low Risk
Investment Cost	High	Low
Operation Cost	Low	High
Principal Criteria	Cleaning Cost	Cleaning Quality

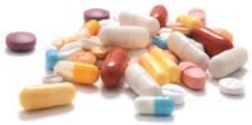
6. Comparison between various types of CIP systems

Single Use CIP

- Low Capital Cost
- Small Space Req.
- Low Contamination Risk
- Total Loss
  - High Water Use
  - High Energy Use
  - High Effluent Vols.
- Longer Time/Delay
- Use for Yeast

Recovery CIP

- High Capital Cost
- Large Space Req.
- Higher Contamination Risk
- Low Loss
  - Low Water Use
  - Low Energy Use
  - Low Effluent Vols.
- Shorter Time/Delay
- Use for Brewhouse & Fermenting



CIP - SIP

6. SIP / CIP / COP ?

SIP : S_____ I__ P_____

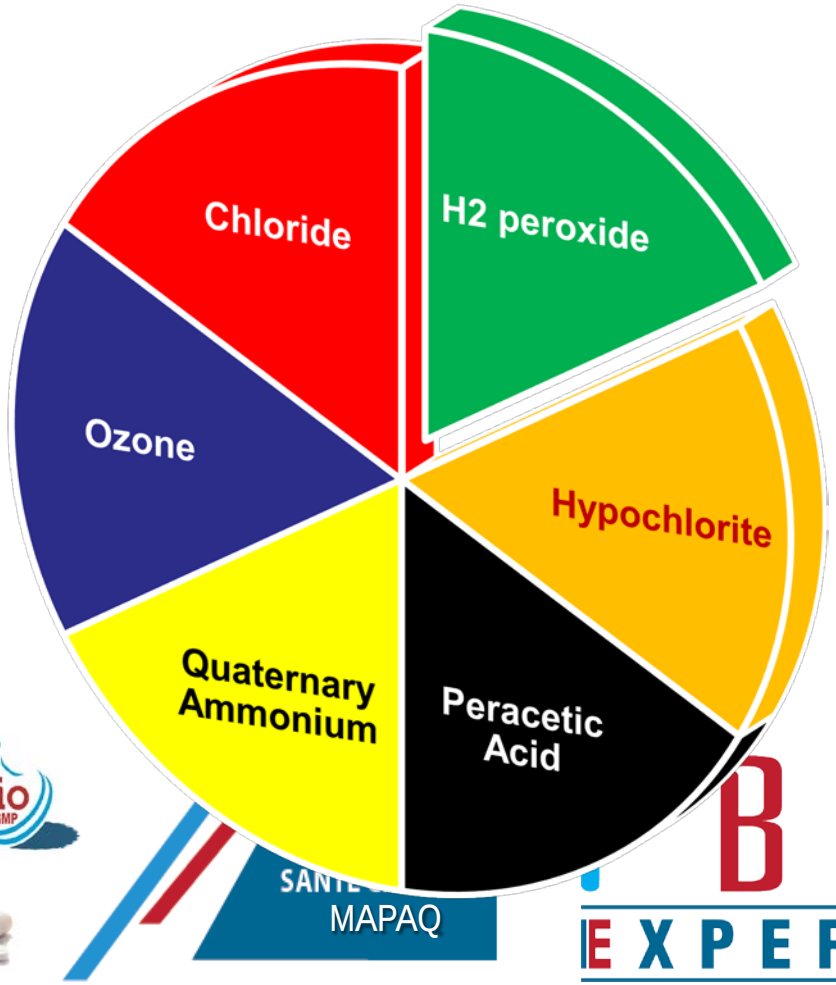
- SIP : Ch_____, Th_____, Fi_____:
  - Washing (____ Log),
  - Disinfection (____ Log),
  - Sanitisation (____ Log),
  - Sterilization (____ Log) of equipment after cleaning
- SEP = Eliminate microbiological contaminants (6Log).

6. SIP / CIP / COP ?

Introduction of the Chemical Sanitization Agent during the CIP Final Rinse Phase.

Chemical Sanitizing Agents:

1. Chloride,
2. Hypochlorite,
3. Peracetic Acid,
4. Quaternary ammonium,
5. Ozone,
6. Hydrogen peroxide.



GEP / Washing Spray Balls

6. GEP / Washing Spray Balls

Spray Devices – Fixed

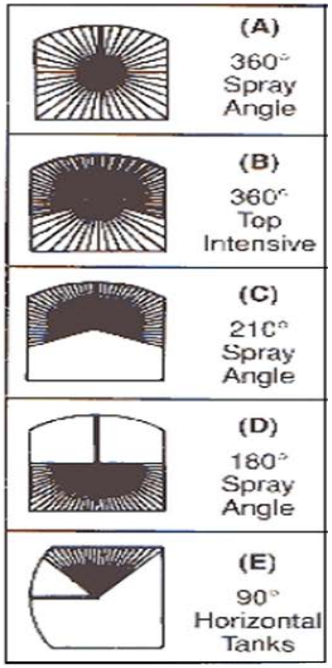
Low Pressure – High Flow

Advantages

- No maintenance
- Special Spray Patterns
- Easier to Monitor
- Less Pump Power

Disadvantages

- Higher Water Usage
- Less Mechanical Action
- Less Bounce Back
- Longer cleaning times



6. GEP / Washing Spray Balls

Table SD-5 Flow Rates to Achieve 5 ft/sec (1.52 m/s)

Sanitary Tube Size						Pressure
O.D.		I.D.		Flow Rate		
in.	mm	in.	mm	gpm	Lpm	(Bars)
0.5	12.7	0.37	9.4	1.7	6.3	-
0.75	19.1	0.62	15.7	4.7	18	-
1.0	25.4	0.87	22.1	9.3	35	-
1.5	38.1	1.37	34.8	23	87	-
2	50.8	1.87	47.5	42.8	162	-

6. GEP / Washing Spray Balls

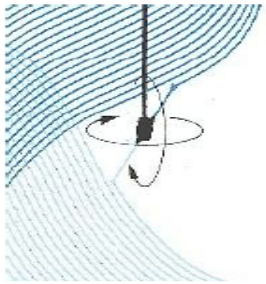
Spray Device – Rotating

High Pressure – Low Flow

Advantages

- Lower Water Usage
- Greater Mechanical Action
- Greater Bounce Back
- Greater Throw Distances

'Turbodisk'

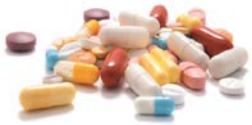


Disadvantages

- Higher Pump Power
- More Difficult to Monitor
- Generally Higher Cost
- More Difficult to "Aim" Spray
- Higher Maintenance

Jets

Slotted



CIP Performance?

CIP Performance?

1. Cleaning Risk Assessment
2. Selection of a CIP unit
3. Sanitary Design
4. Flexibility
5. CIP / SIP : Process Interfaces
6. Optimized length of CIP Loop circuits
7. Supervision, Control to ensure Reproducibility
8. Can be validated

CIP Monitoring Systems

CIP Monitoring Systems ?

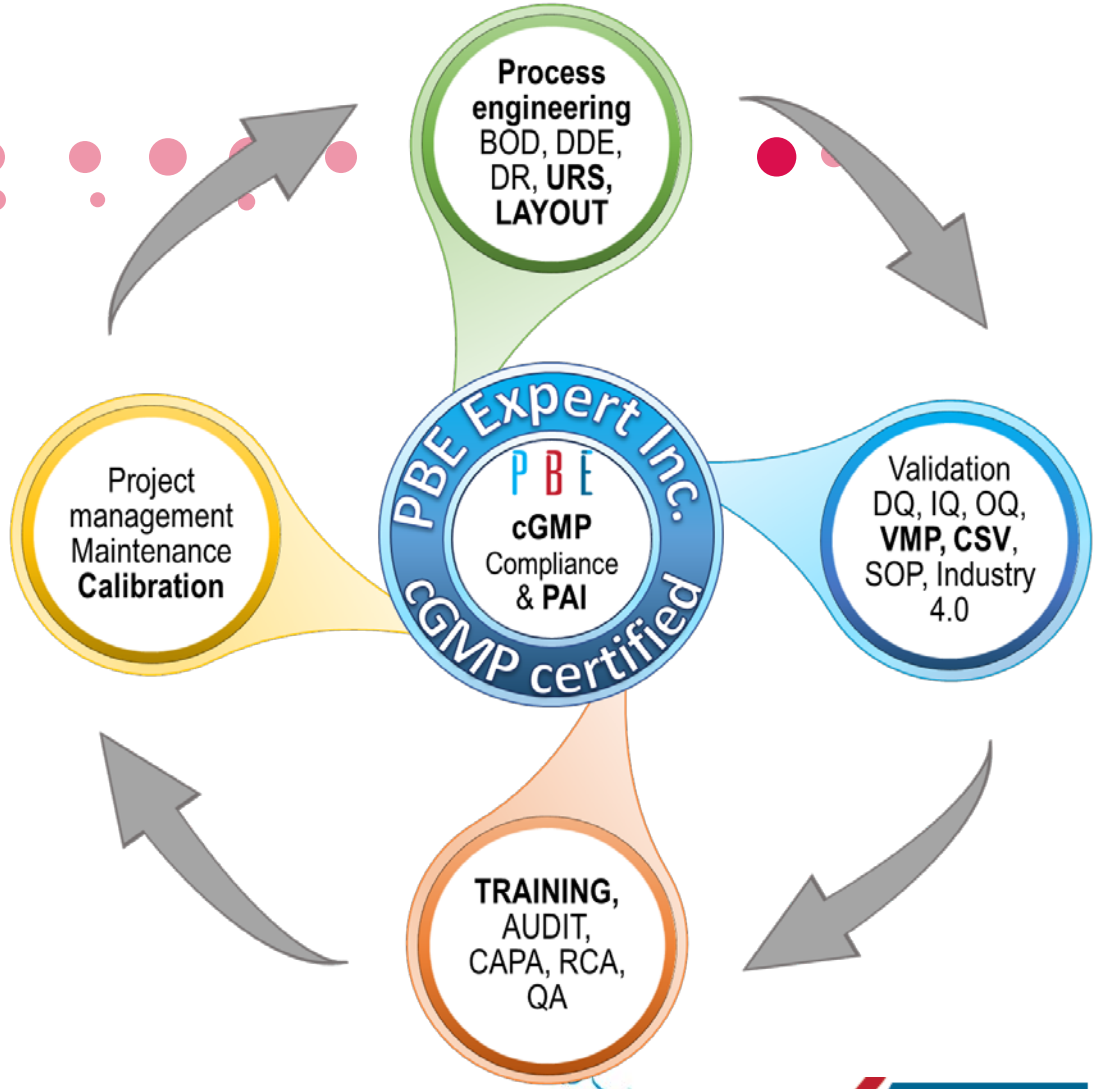
pH, Conductivity	
Temperature	
Flow	
Pressure	
Time	
Turbidity	

Sanitary Design of cleaning processes.

Part 2 - continuing ...

Cleaning validation.

Part 3 - continuing ....



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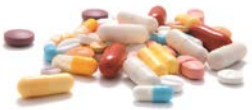

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