CLEAN IN PLACE (CIP) TECNIQUES FOR PHARMACEUTICAL, FOOD AND MILK INDUSTRY: REVIEW

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***Abstract*: Clean in place technique are cleaning the interior surface of enclosed vessel, pipeline circuit, filter housing, filter and associated equipment thing without dismantling or opening the system. It is performing to remove applied residues from complete items of plant equipment. Depending on the type of plant and load of soil residue various cleaningsolution are used like detergent and disinfectant. Clean in place means to circulate the required cleaning solution through the piping and spraying into the vessel with specific time of interval and drained it, rinsed the system with purified water upto specific result and free from previous product as well as soil residue. To get the most effective CIP result, it is necessary to design the production process and the CIP component and circuit simultaneously. It can be carried out with automated or manual systems and is a reliable and repeatable process that meets the stringent hygiene regulations especially prevalent inthe food, drink and pharmaceutical industries.**

***Keywords*: CIP (clean in place), equipment, Device, Cleaning Solution.**

INTRODUCTION

The pharmaceutical and food industry are generally words largest manufacturing sector and influential one of the most stable. Clean in place is unique process doing before the starting manufacturing process in pharma, food, milk and beverage industry to cleaning surface of essentially part of daily operation which comes to contact with products. CIP systems vary widely in configuration, capacity, quality, and level of automation. They also vary by industry. Differences in product characteristics and regulatory considerationsbetween the various processing industries will strongly impact the design of your CIP system. Faulty or wrong process of CIP may cause the health issue and impact on productquality. CIP involves the spraying cleaning solution on surfaces of closed vessles, circulation in pipelines of cleaning solutions through the system under conditions of increased turbulence and flow velocity. It has seen increased demands from customers in terms of CIP verification and validation to provide improvements in plant hygiene,finished product quality, and related shelf-life and microbiological considerations (Tammie, 2008). Depending on the processing practice and load of soiling on the process equipment, the cleaning solutions may be used for single cycle or recycled and reused formulti-use. In multiple use, cleaning solutions are drained after a few to several hundred cleaning cycles.

Equipment of CIP SystemTanks

Tanks are various categories like Manufacturing tank, Holding tank, WFI, Purified water tank, or in milk industry. They are very sophisticated equipment having complex heating and cooling arrangement in jackets to maintain the temperature of vessel. Material use forconstruction of tanks are SS316L and jackets are SS304. The tank made should be suitable for CIP & SIP at regular intervals so as to avoid microbial contamination. The tank should have a close fitting lid, to minimize heat loss, and minimize any solution overflowing the tank.

Pipework

The piping of tank should be suitable for the CIP & SIP. The inlet of water, Air, steam or nitrogen should be connected to the tank. The cooling and heating system connected the outer jacket of the tank or plate heat exchanger fixed by piping. The product piping from bottom of the tank to the pump should connect and from pump it divert in two ways, one is circulation and another is drain or upto the filling machine or other. The recirculation piping is to connect the spray ball or spray device at the time of CIP. The material use for construction of piping is SS304.

Pump-Heart of CIP

It should be sized to provide sufficient flow and pressure to create turbulent flow throughout the piping circuit and also provide the necessary flow and pressure requiredby any spray devices that are installed in tanks or vessels. If a pump is supplying multiple circuits that require different flows and pressures, control of the pump speed with a variable frequency drive (VFD) may be required. The pumps are typically 316 sanitary stainless-steel centrifugal pumps with cleanable seals. The pump elastomers should be compatible with the product soil and cleaning chemicals such as ethylene propylene dienemonomer (EPDM) or a perfluoroelastomer like Dupont's Kalrez®.

Spray Devices

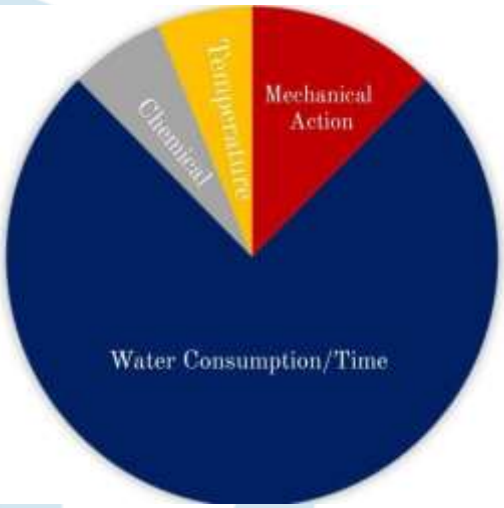
The spray device is worldwide with different shapes, size, configuration and huge range of prices is available. Different shapes size and configuration of device gives different performance. The performance is also dependence on the equipment utilities services

andpressure of fluid, cleaning time, Temperature and turbulence. The spray device is set to the upper centre of the tank with same radius for all side of the tank surface. It gives liquidflow in 360 angle with high pressure to remove the soil or sticky material from the surface. It comes in market with different shapes, sizes and mechanism, depends on its mechanism it gives different name. Each cleaning device and it's mechanism gives it's own advantages and disadvantage. The types of spray device is following-

1. Stationary Spray Device

It is static spray device without moving partsthat just spray the liquid or solution in static manner on the interior surface of the tank to give cleaning result that realies more heavilyon chemical action, the effect of temperature and the duration of the cleaning process Thetheoretical turbulence of the free falling film is only slightly above the laminar flow (1000 < Re < 2000), and the wall shear stress τw is from the order 2-3 Paat 60°C. There are stationary tank cleaning devices that may supply higher amounts of mechanicalenergy in pre-defined areas, and the rest of the tank will still only be cleaned at low shear stress where rather soaking action is taking place. The best well- known tank cleaning devices in this category are static spray balls and Stationary "cluster" spray device.

Stationary Spray Device

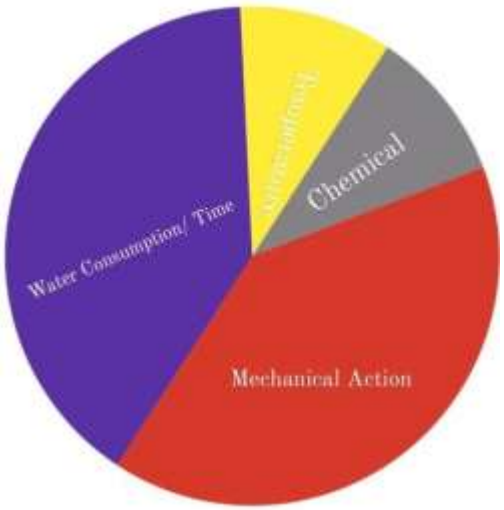


Pie Chart From alfa laval

2. Rotary Spray Devices

Rotary spray device is consisting of either a rotting disc, ring or ball provided with strategically drilled holes, ports or slots that rotates around just one axis. The liquid passed into the smaller number of drilled holes that have higher radical velocity, resultingis more impact on the surface of tank hit the droplets on tank wall. Increased theturbulence of liquid solution impact coverage of interior tank surfaces hence mechanical action is provided then enhanced impact of the cleaning hitting the wall and partially by the gravity assisted low to medium turbulence (2100 to 6000) flow of liquid on thesurface of the tank.

Rotary spray devices

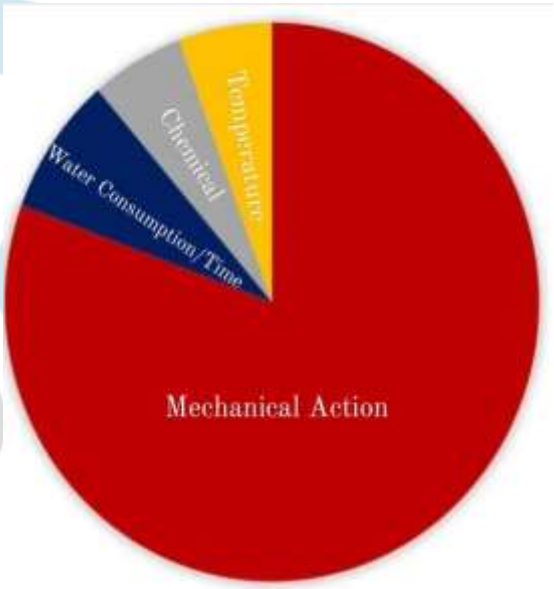


Pie Chart From alfa laval

3. Rotary Jet Device

The rotary jet device consisting 1,2,3,4 or more nozzle are driven by fluid (turbine type) or motor(electric). It rotate around their horizontal or vertical axis while producingsynchronized water stream. Rotary jet device produce scouring pattern upon the internal surface of the tank or vessel. Another type is piston driven particularly manufactured by Breconcherry, acquired by GEA Tüchenhagen Rotary jet devices having high impact on the tank surfaces in 360degree rotation with in tank and having volume in the 15-1250m3range of tank. Some rotary jet devices driven 180 degree taken only upward, downward impingement cleaning. Those who are driven 180 degree only downward direction it isonly for open top vessle and it clean tank side wall and bottom of the tank.

Rotary jet Device



Pie Chart From alfa laval

21CFR

The Code of Federal Regulations (CFR) is a set of rules published by the U.S. government. Title 21 of the CFR (CFR21) is used by the Food and Drug Administration to establish requirements for the manufacture of food industry products and pharmaceuticals, including how equipment should be cleaned and maintained. A top quality, well-designed CIP system should adhere to these guidelines and should comply with CFR21.S88 In recent years a set of standards known officially as ANSI/ISA-88 was developed to address batch process control procedures and provide standard organization for how systems communicate and work together. A CIP system that complies with S88 would have an advantage when it comes to integrating into a process system

SCADA (supervisory control and data acquisition)

Supervisory control and data acquisition (SCADA) is system made by the software and hardware. It is operating with coded signals over communication channels so as to provide control of remote equipment. SCADA gathers information (such as ON the pump)transfer information back to the central site, carry out any necessary analysis and control and then display that information in a logical organized fashion on a number of operator screens or displays. A Programmable Logic Controller (PLC) is a solid state computerized industrial controller that performs discrete or sequential logic in a factory environment. The Technical Definition of a Programmable Logic Controller is currently defined by the National Electrical Manufactures Association (NEMA) as a "digital electronic device that uses a programmable memory to store instructions and to implemented specific functions like logic, sequence, timing, counting and arithmetic operations to control machines and processes".

General CIP Process

The process of CIP System is unique as per its own organization guidelines. So there is no such thing as a typical CIP cycle. The time duration, sequence of chemical, use of chemical, elements can vary widely from one system to another but some common step are included in in most cleaning cycle. Pre Rinse- use de-ionized water, potable plant water, water that has been processed through reverse osmosis or water for injection. Takesufficient water in the tank and recirculate via spray ball to wet the interior surface of the pipeline, tanks and remove the most of the remaining residue or dissolve chemicals. The pre-rinse is a very important step in the CIP process because a well-monitored and well- executed pre-rinse makes the rest of the wash cycle predictable and repeatable.

Caustic wash
The caustic wash or detergent wash to removes organics like protein and fats. Take wateradd sufficient alkaline detergent recirculate via spray device in the tank and flush it.

Intermediate wash
Fresh water flushes to remove the traces of detergent wash

Acid Wash
Dissolves mineral scale from hard water deposits, protein residues, and neutralizes thesystem pH.

Final rinse
Use the fresh water to remove all traces of cleaning chemical recirculate through spraydevice and flush it. It do several times still the tank free from cleaning solution.

Chemical Basis Alkaline

The alkaline detergent that have very high pH typically used in concentration range of 0.5-4.0%. It exhibits excellent removal of proteinaceous soils and fatty oils by saponification. These are usually consist of sodium hydroxide (caustic soda) potassium hydroxide (caustic potash), sodium carbonate (soda ash), and sodium silicates. Tri sodium phosphate (TSP) is also placed into the alkali group because of its reaction with water to yield hydroxide.

Acid
The acid detergent that have lower the pH typically used in concentration range 0.5- 3.0%.Dissolves mineral scale from hard water deposits, protein residues, and neutralizes the system pH. Acid is also excellent for brightening up discolored stainless steel by removing calcified mineral stains. Acids must be used with caution because they can attack some elastomers in the system like gaskets or valve seats, causing premature degradation or failure. They are usually consist of phosphoric acid, Nitric acid, hydrochloric acid, hydroxyacetic acid, gluconic Acid etc.

Instrumentation
The following instruments recommended for a cleaning system

Flowmeter- To collect the specific amount of water in the tank

Pressure gauges- To measure the pressure of different places like on the tank during SIP,Recirculation pipe, product pipe, filter housing etc.

Thermometer- To measure the temperature during manufacturing process, SIP , CIP ofthe tank.

pH & conductivity meter – To monitor the pH during the manufacturing process and maintain it. During CIP to check the pH and conductivity of the previous product traces till it get satisfactory result

CIP Validation
Validation of a CIP system is a demonstration, to a reasonable degree of assurance, that cleaning according to a specified SOP will actually attain the required level of cleanliness,including removal of cleaning agents, in a reproducible manner. Cleaning validation guidance given by the FDA 2004, “Guide to Inspections Validation of Cleaning Processes.” “FDA expects firms to have written procedures [Standard Operating Procedures (SOPs)] detailing the cleaning processes. In the clean in place validation protocol mention all objective, safety measure, sampling and testing of cleaning validation. In the cleaning validation process visual inspection, surface sampling, rinse water sampling and it’s testing carried out. In visual inspection to check the surface of the tank and take surface sample may or may not residue adhere to the surface of tank check. Rinsed water sampling and test analysis can be quantitative, using pH, conductivity, particle count, microbial count (Bioburden), Total Organic Carbon (TOC) determination, spectro photometry, bioassays, or limulus amebocyte lysate for pyrogens. Finally todetermine or examine rinsed sample residue by the different method HPLC, UV, titration,enzymatic detection and flame photometry to detect which traces present in the residue. These procedures will “address who is responsible for performing and approving the validation study, the acceptance criteria, and when revalidation will berequired.”

Conclusion
Clean in place system in pharma industry, Food industry, Dairy plant various types of cleaning solution, detergent and method of cleaning changes by the organizational guidelines. The instrument, equipment design installed as per DQ, IQ, OQ & PQ protocol, the protocol made by the project expert as suitable for it’s operation. The above information is general structure and process of CIP it may differ by the organizational guidelines. The validation of the CIPs should be timely revise by changing any process orequipment in CIP system to obtain good quality product.

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