

## TIPS FOR GOOD SANITATION AND HYGIENE PRACTICES IN PHARMACEUTICAL MANUFACTURING

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He is associated with Perfect Pharmaceutical Consultants Pvt. Limited and Global Institute of Regulatory affairs (Pune, India). He is dedicated solely to the continuing education for regulatory professionals. This article is solely written to guide, educate and train regulatory community at large in the field of sanitation and hygiene at work place.

This article is based self experience of 25 years of the author

### Background:

Every pharmaceutical site needs good hygiene and sanitation over 24 hours and 365 days a year. As per my personal experience the 70 % of the failure in sanitation and hygiene can be attributed to the lack of orientation and inadequate training. It is very commonly observed that the cleaning records are filled mechanically.

Followings are the critical areas for sanitation and hygiene.

No	Critical Areas which needs active attention for Cleaning and sanitation
1	Store areas where Excipients such as sugar, lactose and starch are stored in large quantities
2	Liquid Processing areas
3	Equipment washing areas
4	Water handling systems
5	Containers /closures cleaning and storage areas
6	Personal Wash Rooms and Primary Change Rooms
7	Refreshment and Lunch rooms
8	Materials receiving areas
9	Sanitary and Product drain lines
10	Air handling systems
11	Sampling and dispensing areas
12	Service areas
13	Processes involving high dusting
14	Packaging areas
15	Corrugated Boxes storage area
16	Open electrical wirings, electrical lamps, and open service lines
17	Ledges and platforms

The article has been written with the audit point of view. It provides critical guidelines for securing good sanitation as well as it highlights the bad practices which need to be controlled.

No	<b>GOOD PRACTICES (ENSURE IT)</b>	<b>BAD PRACTICES (AVOID IT)</b>
1	Ensure that the premise is neat and clean and is free of pooled water.	<i>Premise is uneven, untidy, wrongly sloped to deposit dirt and rain water towards main production blocks</i>
2	Ensure that there are no harborages and breeding areas at the site	<i>Pooled water , open water wells and water tanks , open garbage stores, scattered scrap material, damp areas with insect harboring</i>
3	Ensure that incoming material unloading/loading areas are properly constructed and protected	<i>Unloading /loading areas are grossly untidy. Muddy and dusty</i>
4	Ensure that Approved pesticides are used as per SOP	<i>Pest harboring places and pest burrow present. No pest control system in place</i>
5	Ensure that walkways are cemented	<i>Muddy and dusty walkways</i>
6	Ensure that there are Cemented roads for transportation	<i>Uneven dusty Transportation area</i>
7	Ensure that Properly closed areas are used for storage of waste materials	<i>Waste materials scattered at backyard</i>
8	Ensure that the Green areas are located away from main building.	<i>Uncontrolled growth of plants/weed/ grass and open drain lines</i>
9	Ensure that no pets are housed in the premises	<i>Pet housings provided</i>
10	Ensure that the floorings are Smooth (Polished) and does not allow collection of dust	<i>Flooring s are Rough , allows collection of dust and supports microbial flora</i>
11	Ensure that Floorings are Impervious and Continuous (preferably epoxy coated)	<i>Flooring allows seepage of water /potholes present</i>
12	Ensure that Floorings are Suitably leveled. The cables, water pipes and gas pipes are concealed.	<i>Uneveled flooring, Open drains, Open Electrical cables and water lines</i>
13	Ensure that the floorings are sloped to self drain the spilled water or washings	<i>Sloped to retain the spilled water</i>
14	Ensure that Walls and Ceiling of Production Area are routinely cleaned and sanitized	<i>No cleaning done</i>
15	Ensure that Covings are provided at wall, ceiling and floor Joints	<i>Angular joints</i>
16	Ensure that the Walls and Floors are Washable	<i>Walls are Non washable</i>
17	Ensure that the walls are Light Colored to check dust/bacterial invasion of any kind	<i>Walls are Dark colored ( even crawling insects can not be easily detected)</i>
18	Ensure that the walls and flooring are maintained in Good Repair	<i>Walls and floorings are in Bad repair as evident from peeling of paint, discoloration and nailing holes</i>
19	Ensure that walls are smooth and not prone to catch dust.	<i>Walls are Rough. Prone to retain dust. Difficult to clean.</i>

20	Ensure that all main openings of production area are effectively protected against entry of flies, mosquitoes and rodents.(Air Curtains Provided/ Mosquito electrocutor provided)	<i>No Air Curtains on main entries. No electrocutor provided</i>
21	Ensure that bottom and top of doors and windows are sealed	<i>Bottom, tops and sides are not sealed. Insect, mosquitoes and dust entry freely possible</i>
22	Ensure that main outdoors are self closing	<i>Outer door need manual closing. It remains opened many a times</i>
23	Ensure that the outer doors are protected by screen doors.	<i>There are no screen doors. Any person can just open and enter any time through the main door</i>
24	Ensure that the access control system is provided on outer doors as well as critical internal doors	<i>No access control system or guard is provided. Access is direct. Just push and enter any time.</i>
25	Ensure that Proper Lighting is provided to check the cleaning status of area and equipments	<i>Inadequate lights in gangways. Inadequate lighting on and around the machines. The hazardous and dangerous points are not clearly visible. Inadequate light on switchboards and control panels. The batch identification details displayed are poorly readable</i>
26	Ensure that Flame proof light fixtures are provided in inflammable storage/processing areas. Ensure that the mobile handsets are prohibited in such areas.	<i>Solvent storage, handling and application areas are not supplied with Flame proof fixtures. High voltage supply is not properly guarded by flame proof cables and light fixtures.</i>
27	Ensure that the Lighting fixtures/Cables are concealed in wall or roof.	<i>Open Light Fixtures</i>
28	Ensure that the Lighting switches are outside the processing area	<i>Lighting Switches are inside the processing areas</i>
29	Ensure that when cables are running through the walls, the entry and exit points are properly sealed	<i>Entry and exit points of cables/pipe lines through the wall are not sealed properly. The openings provide ideal location for harboring of insects.</i>
30	Ensure that Earthing is provided to each and every instrument Lightning arrester is provided at the top of the establishment. Earthing points are well maintained.	<i>Earthing system for electrical supply is not sound.</i>
31	Ensure that AHU/HVAC system is designed suitably	<i>AHU system is not properly designed and installed.</i>
32	Ensure that exhaust ducts are provided with filters and the ends are suitably protected	<i>Exhaust duct are open to environment and allows entry of insects, birds and dust</i>
33	Ensure that suitable air pressure gradient is maintained in critical areas.	<i>The pressure gradient is in wrongly designed. The external contamination enters in clean room.</i>

34	Ensure that HVAC system is capable of maintaining required Humidity, temperature and pressure in AAAS (all areas and in all seasons	<i>The system fails during peak season.</i>
35	Ensure that the sanitation of ducts is maintained	<i>HVAC ducts are rarely cleaned. The access to the system is limited. Proper cleaning points are not provided.</i>
36	Ensure that the risers are provided at ground level to effectively exhaust the contaminated air	<i>Risers are not provided. The exhaust ducts are located in the ceiling of the room.</i>
37	Ensure that there is no direct or indirect connection between process and product water. Only the cleaned water is supplied to the production areas.	<i>Process and Product water lines are intermixed. The process water outlet is connected to product water inlet during shortage of water</i>
38	Ensure that the dedicated system for treatment and storage of Product water is in place.	<i>The product water shows seasonal variation in quality. Raw Water storage system is rarely cleaned and sanitized. The final product water is stored at ambient temperature without recirculation</i>
39	Ensure that there is separate storage, supply and drain system for Process water	<i>The process water system is not dedicated. There is indirect connection with product water. In case of shortage the process water is intentionally used for manufacturing products.</i>
40	Ensure that the Product water system is duly validated to cover all seasons and extreme feed water quality	<i>The Product Water system is inadequately validated. The system goes out of order during summer when there is water shortage and during rains when the water quality is very low.</i>
41	Ensure that separate rooms are provided for storage of Excipients/API/potentially toxic ingredients/ Sterile ingredients/ Finished products/ semi finished products/ Packaging materials/ under test materials/rejected materials/ released materials/Thermo labile materials /Engineering materials / Spares /Inflammable materials/ Records and Reports. Each area is properly cleaned and sanitized.	<i>One common area is provided for storage of all kinds of materials. Under test and Tested materials are intermixed. The gangways and passage is utilized for storing surplus materials.</i>
42	Ensure that the toilets doors do not open directly into production areas or service areas.	<i>The sanitary rooms directly opens into process areas and service area</i>
43	Ensure that wash rooms are clean, well-lighted and ventilated	<i>The sanitary block is not well lighted. The whole area is off smelling. The entry of birds/insects/lizards is evident from window openings.</i>

44	Ensure that sewage and sanitary lines are separate.	<i>Sewage and sanitary waste lines are broken and water pool is observed in the connected areas.</i>
45	Ensure that Sanitary Doors are of tight fit type and are self-closing	<i>Sanitary doors don't fit properly. The doors are manually operated and hence remains open accidentally</i>
46	Ensure that adequate Hand washing facilities are provided and equipped as required	<i>Hand washing facility is very poor. The taps are very hard to open and close. They are not conveniently reachable. Lot of strain is caused on the body to access the same. The water is off smelling</i>
47	Ensure that hand washing facilities are Clean and in good repair condition	<i>Water pooling is observed around the wash facilities. The same facility is used for equipment washings in emergency. Trash deposit is observed around the facility.</i>
48	Ensure that Sanitary pipes ( SS 304 or SS 316 ) and fittings are used for water system	<i>Sanitary pipes are made of plastic, joints are inadequately sealed and plaques were observed near the joints.</i>
49	Ensure that the Hands are thoroughly washed while entering the production areas and rewashed when contaminated	<i>Hands are washed while entering the area. They are not rewashed when get contaminated during operations.</i>
50	Ensure that Cleaned outer garments and hair covers are provided to all production employees.	<i>Outer garments are reused without cleaning. No adequate cleaning facilities available at site. No contract services are available for regular washings.</i>
51	Ensure that tobacco and food materials are not consumed in production areas. A separate dedicated area for smoking, chewing and food is provided outside the manufacturing premises.	<i>Use of tobacco ,food material and smoking was evident in process areas</i>
52	Ensure that Clean boot covers, cap and coverall is worn when entering in the manufacturing area.	<i>The most of the people were observed bare head without any cap.</i>
53	Ensure that all equipments and vessels are maintained in covered state when not in use	<i>The containers and vessels were observed without proper lids</i>
54	Ensuring Cleaning And Sanitizing Of Containers And Equipments is done regularly	<i>Dedicated facility for cleaning the containers and equipments not provided</i>
55	Ensure that Fully validated CIP system is used wherever possible	<i>The equipments are cleaned manually. The cleaning system is not validated.</i>
56	Ensure that no routine cleaning activities are performed during manufacturing Ensure that hard to clean devices such as stirrers, sieves, pipelines and valves are effectively cleaned and cleaning processes are validated.	<i>No fixed schedule for cleaning  The stirrers, sieves, services pipelines and valves are often neglected for cleaning.</i>

57	Ensure that all persons employed for manufacturing are in good health Ensure that no person with open wound/lesions is allowed to handle any material/vessels.	<i>No effective control on the health conditions.</i>
58	Ensure that all the operations are performed using cleaned garments, hand gloves and face/hairs mask. Direct contact between product and operator is avoided	<i>Direct entry with street clothes.</i>
59	Ensure regular cleaning of Walls, floors, ceilings, ledges, drains, air supply ducts, air bags, air filters, machine hoods and platforms	<i>Occasional cleaning of only easily accessible areas and surfaces.</i>
60	Ensure that AHU/HVAC system provides clean air of proper temperature and humidity. Ensure that Proper Pressure differential is maintained across clean and unclean areas.	<i>Random air flow pattern, undefined pressure differentials</i>
61	Ensure that water system is Properly designed and duly validated for performance over all seasons.	<i>Water system poorly designed. Dead legs present</i>
62	Ensure that the cleaning of equipments and areas are properly managed and the cleaning methods are properly validated.	<i>Cleaning operations are performed but not suitably validated</i>
63	Ensure that all incoming materials are suitably decontamination before entry to stores	<i>The material enters directly into stores</i>
64	Ensure that the manufacturing system is duly protected for cross contamination at every stage	<i>Partially/Fully open processing system. Hence chance of cross contamination</i>
65	Ensure that the Walls, floors, ceilings, ledges, drains, are designed to prevent collection of product dust	<i>The building is wrongly designed to include corners, underneath spaces, ledges, holes and platforms which promote collection of dust.</i>
66	Ensure that the entire production area (inch to inch basis) is effectively cleaned on routine basis	<i>Occasional cleaning of areas.</i>
67	Ensure Sanitation of Critical Contact parts of machine	<i>The machine contacts parts are ignored for cleaning</i>
68	Ensure sanitation of obscured locations Ensure adequate sanitation and cleaning of AHU ducting's	<i>Obscured locations ignored AHU are not maintained and cleaned after installation.</i>
69	Ensure Sanitary Storage Of Cleaned Containers And Equipments	<i>Clean containers are stored open to environment</i>
70	Ensure dedicated product water and steam lines	<i>Cross connections between process water and product water/ process steam an product seam</i>
71	Ensure that transportation vehicles are clean and sanitized	<i>Vehicles are highly unhygienic.</i>

72	Ensure that the Vehicles are Constructed to protect the products from environmental dust	<i>Vehicles allow dirt/dust during transportation</i>
73	Ensure that manufacturing areas are designed so as to preclude undue microbial contamination from operations and environment	<i>No attention on bioburden</i>
74	Ensure that the containers, equipment, service lines and utensils are sanitized before and after using live steam.	<i>No effective sanitation practices</i>
75	Ensure that fumigation is done in clean areas as per SOP	<i>Fumigation is rarely done</i>
76	Ensure that the entire facility is cleaned and sanitized daily. The spillage is controlled	<i>Only few selected areas are cleaned and sanitized daily.</i>

**Conclusion:** Sanitation and Hygiene is a very delicate component of cGMP. More you define more it becomes complex. You never know where to limit your SOP .It shall be practiced with meticulous care and sincerity. It shall never happen that you site is rejected before inspection. There are numerous examples where Pharma sites have been rejected by FDA just at glance on change room and toilets facilities.