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Cleaning Validation of Different Laboratories of Rajarambapu College of Pharmacy Kasegaon

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ABSTRACT

Pharmaceutical product and active pharmaceutical ingredients (APIs) can be contaminated by other pharmaceutical products or APIs, by cleaning agents, by microorganisms or by other materials e.g. airborne particle, dust, lubricants, raw materials, intermediates. Mainly cleaning is performed to remove product and non-product contaminating material. Ineffective cleaning can lead to adulterated product, which may be from previous product batches, cleaning agent or other extraneous material introduced into generated by the process. In many cases, the same equipment may be used for processing different products. To avoid contamination source or facility configuration there is a need to ensure that cleaning procedure must strictly follow carefully established and validated method of execution.

INTRODUCTION

Validation is documented evidence which provide a high degree of assurance that a specific process will consistently produce a product meeting its predetermined specification and quality attributes.

Cleaning validation is documented evidence with high degree of assurance that one can consistently clean a system or piece of equipment to predetermined and acceptable limits. Cleaning validation is primarily applicable to the cleaning of process manufacturing equipment in pharmaceutical industry. It is necessary to have effective cleaning programs in place because of regulatory requirements.

Proper cleaning as per cleaning SOP's and followed by protocol of cleaning and proper techniques of cleaning is essential for pure and contamination free environment produced in college. However more fundamental reason is that to perform practical pure and free from contamination to extent that is possible and feasible to give better result.

Definition Of Cleaning Validation:

Cleaning validation is documented evidence with high degree of assurance that one can consistently clean a system or equipment to predetermined and acceptable limits.

Why Cleaning Validation:

To verify the effectiveness of cleaning procedures and to ensure no risks are associated with cross- contamination of active ingredient or detergents/sanitizer.

When Cleaning Validation:

1. Initial qualification of process/ equipment.
2. Critical change in a cleaning procedure.
3. Critical change in formulation.
4. Significant change in formulation.
5. Change in a cleaning process.

6. Change in a cleaning agent.

Advantages of Cleaning Validation:

1. Safety**:** Validation can also result in increased operator safety. Properly calibrated, validated instruments and gauge used to reduce accident and results in safety.

2. Better result quality: Through proper validation, performed practicals gives better result without any of the cross contaminated equipments and apparatus.

Contamination & Cross-contamination

Generally cross-contamination and contamination by a foreign material are two types of contamination. Cross-contamination is usually through an active ingredient from one product carrying over into subsequent manufactured product. However, carryover of other product component such as excipients can also be problematic and may degrade and final quality of product. Contamination of one batch of product with significant level of residual active ingredient from a previous batch may pose obvious problem to consumer or patients from unintended contaminants.

Potential clinically significant synergistic interaction between pharmacologically active chemical is a real concern. Inert ingredients used in drug product are generally recognized as safe for human consumption and for routine use also. Maintenance and cleaning of equipment provide the potential for contamination with items such as equipment parts and lubricant. Chemical cleaning agent and piece of cleaning tools can cause problems ranging from poor pharmaceutical elegance to exceeding acceptable levels of particulate matter in parenteral products to inadvertent inclusion of toxic compounds in the product. In addition, some activities are adversely affected by trace contaminants and may exhibit change in stability or bioavailability if exposed to such contamination.

The second type of contamination is by foreign material these may be bacterial in nature or could represent part of the equipment. Maintenance, cleaning, and storage condition may provide adventitious microorganisms with the opportunity to proliferate within processing equipment. This could pose obvious problems for sterile products manufacture (generation of high level of pyrogens, decreasing the assurance of sterile achieved by equipment sterilization procedures etc.) It also possess serious problem for the manufacture on nonsterile dosage form

particularly unpreserved products which support microbial growth.

Mechanism of Contamination:

1. **Cross contamination with active ingredient:**

One of the real dangers in cross contamination of active ingredients is that by being contaminated results in a multiple ingredient product instead of single active ingredient. Depending on medical effects, the contamination may enhance the action or neglect the action or contaminant may have an entirely different medical effects.

2. **Microbiological contamination:**

This form of contamination is particularly insidious because the contamination may develop at any time, even after cleaning. A major contributing factor is the storage of equipment in a wet condition. This provides a natural medium in which bacteria can grow.

3. **Contamination by cleaning or sanitizing agents :**

Some pharmaceutical operations may find it necessary to use fairly toxic materials for cleaning purpose for stubborn residues. This is particularly true in the manufacture of active pharmaceutical ingredients (APIs). As such, these materials represent a potential threat as contaminants. It seems obvious that one effective way of dealing with this potential problem is to use cleaning agents with the lowest toxicity that will still be effective in removing the residue in the given cleaning situation. The same factors also apply to sanitizing agents used to wipe down cleaned equipment.

4. **Contamination by miscellaneous other materials:**

In addition to the usual expected or anticipated list of potential contamination in a pharmaceutical operation, many other less likely materials can also contaminate products. A partial list includes equipment parts such as excipients, bristles from brushes used in packaging filling equipment, paper filters, micron filters, fibers and rubber particles from gloves, cleaning aids such as brush bristles, cloth, and cotton fibers from rags and wiping materials, lubricants.

Equipment/Laboratory characterization:

Cleaning validation involves not only the removal of residues but also gives assurance that

each and every piece of equipment associated with the process has been cleaned to acceptable levels. It is typically referred as train based approach. The equipment train is series of equipment through which the product or products move as they progress through the Manufacturing process.

In order to asses that the equipment is cleanable or not it should be characterized in such a way that its design features are well known. Equipment characterization can assist cleaning validation initiatives in many ways:

1. Promote more effective cleaning procedure by identifying cleaning challenges and ensuring that they are addressed in the cleaning methods employed.

2. Identifying hard to clean locations and high-risk locations in equipment for the purpose of sampling site selection.

3. Target materials of construction that will be included in sampling recovery studies and those that will not be included.

4. Isolate materials that will be disposed of at the end of a production process and/or will be dedicated to a single product.

5. Verify that all materials of construction are compatible with the selected cleaning agents and temperature that will be used with the cleaning process.

6. Collect product contact and sample site surface areas for the purpose of calculating limits and results.

7. Confirm similar geometries, capacities, and use of process equipment for the purpose of grouping that equipment.

Note:

When performing correctly, equipment characterization is the process whereby it catalogues the features and attributes of equipment, thereby ensuring that equipment can be cleaned reliably and reproducibly.

Cleaning Agent selection:

Cleaning chemistries fall into several broad categories;

1. Water
2. Solvents
3. Commodity chemicals
4. Formulated cleaning agents

1. **Water:**

It is the universal solvent. If water alone will effectively clean the lab's without undue time or physical effort to remove the residues, by all means employ water alone. For many, however the water alone requires an unacceptable increase in time to get the cleaning accomplished. For these individuals, one of the other approaches must be sought.

2. **Solvent:**

These are typically applied in processes where solvent usage is already called for by the manufacturing process. For example, mother liquors are typically used as the solvents for cleaning of APIs. As the mother liquors is already known to dissolve the primary residue, there is little risk in employing if for cleaning.

3. **Commodity chemicals:**

In this, chemicals **s**uch as NaOH can be used for cleaning as well. Like their solvent counterparts, there may be hazard issues, effluent issues associated with these materials. Their typically high alkalinity or low acidity, however, often makes them helpful in inactivation processes. However these chemicals lack the detergency of a formulated cleaning agent and they may be difficult to rinse, taking larger volumes of water to rinse free from systems than would a formulated cleaning agent.

4. **Formulated cleaning agent:**

It is the largest class of cleaners. This category includes solvent-based formulations and aqueous formulations. Typically formulated cleaning agents can include one or more alkalinity or acidity sources, surfactants builders, sequestrants, chelants and either a solvent or water. For industrial applications, unlike consumer-use products, these materials are formulated to be low foaming and therefore are more readily rinsable and are appropriate for high impingement or

high turbulence cleaning.

Cleaning Validation Program

a) Selection of cleaning Level (Type)

b) Selection of cleaning method

c) Selection of sampling method

d) Selection of scientific basis for the contamination limit (acceptance criteria)

e) Selection of Worst case related to the equipment

f) Selection of Worst case related to the product

g) Establishing the storage period after cleaning (hold time study)

Selection of analytical method

h) Documentation

METHODS OF CLEANING

1. Choice of disinfectants

Use of disinfectants in combination with more than one disinfectant as the use of single disinfectant possibility of development of resistance by microorganism's use of disinfectant in combination will avoid development of resistance.

2. Frequency of cleaning

Frequency of cleaning previously was once in day after implementation of collaborative cleaning procedure it is change to 2-times a day .The concentration of disinfectant is 2.5 %.

3. Concentration of disinfectants

The concentration of disinfectant must be 2.5 % which is implemented.

Correct Methods For Cleaning:

-

Figure 1: Correct Wiping Method (step 1)

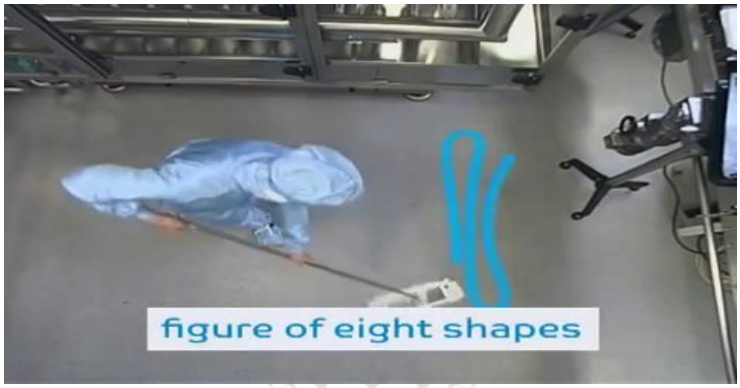


Figure 2: Correct Wiping Method (step 2)

Figure 3: Correct Wiping Method (step 3)

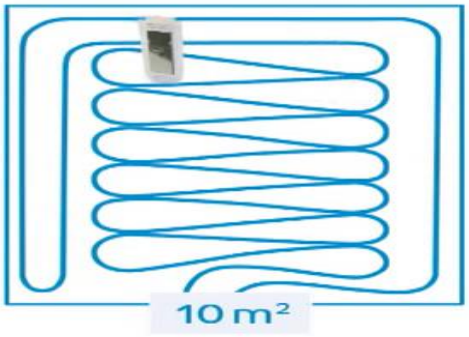


Figure 4: direction of wiping (step 4) **Figure 5: Angle for wiping (step 5)**

Validation protocols should contain

a) Purpose of the validation study

b) Responsible person for validation study, like performer and approving authority

c) Full description of equipment to be used in cleaning which include list of equipment, make model, capacity

d) The cleaning cycle and their frequency for any equipment before and after use

e) Detailed list of all critical steps to be monitored

f) Selection of cleaning agent with all detail like solubility of material to be cleaned, safety , product removal limit, minimum temperature and volume of cleaning agent

g) Detailed Sampling procedure

h) Type of sampler

i) Volume/quantity of sample

j) Containers for sample

k) Sampling location

l) Sample handling

m) Sample storage

n) Analytical testing procedure with LOD (limit of detection)

o) The rational acceptance criteria with margin of error and sampling efficiency

p) Change control

q) Approval of protocol before the study

r) Deviation

Cleaning agent:

Cleaning agent is used for cleaning purpose; it may be a combination of detergent and water or other agent like chelating agents. It should have high solubility towards the product to be removed. The properties of cleaning agents are given below:

a) It should not degrade the product.

b) It should be compatible with the equipment.

c) It should not cause environment hazardous.

d) It should not be a contaminant of subsequent product.

e) It should easily removable and easily available and nontoxic.

Some example of solvent given below-

1. Water is universal solvent which is used in combination with surfactants.

2. Organic solvent like acetone, methanol, ethyl acetate are also used.

3. We can use aqueous solution of sodium lauryl sulphate or sodium dodecyl sulfate.

4. The chelants solvents can also be used (ethylenediaminetetraacetic acid, nitrilotriacetic acid, sodium hexa meta phosphate /base sodium hydroxide, potassium hydroxide).

5. We can also use some acid for example glycolic acid, citric acid etc.

6. The oxidant can also be used for example sodium hypochlorite, hydrogen peroxide.

Used solvent For Cleaning:

Actually solvent used for cleaning is commercially used for cleaning is Lysol , Dettol , Cresol, Phenyl .

Personnel for cleaning:

Personnel involving in cleaning procedure should be trained. Training should be recorded. The person should have suitable working clothing to prevent spreading the particles and dust. The direct contact between personnel and products should be avoided.

Design and construction:

The buildings should be designed to minimize the potential contamination whether it is a cross contamination or microbiological. Therefore the designing and location of buildings and facilities should be constructed to facilitate the easy cleaning and easy maintenance. All parts of the equipment and area can be easily washable to minimize or reduce the chances of deposition of contaminants on broken parts, groves and open joints of equipments. The methods, critical parameter like cleaning frequency and number of cleaning cycles and cleaning procedure must be validated.

Cleaning of Area

The area shall be cleaned according to the following types:

Type A cleaning for area

The whole room from ceiling to walls progressing to downwards including pallets, SOPs stand, accessories box weighing balance, air handling unit (AHU) supply/return grilles switchboards, utility pendants should be cleaned by using the vacuum cleaner and wiped with vacuum

cleaner. Then the waste materials are collected, put into suitable poly bags and tied up, then accordingly labeled and sent to the scrap area. The entire room is cleaned with potable water and rinsed with de-mineralized water, and then dry duster is applied, and cleaned with disinfectant solution using wet duster or lint-free cloths. All item present in room are mopped with dry duster and then with wet duster using disinfectant solution. The drain points are cleaned and sufficient volume of disinfectant is poured. The whole cleaning activity should be recorded in the cleaning record log book and specific log book of item present in the room.

Type B cleaning for area

All the dust and gross accumulations from equipment and area removed**.** Then the waste material is collected and put in suitable poly bags then tied up, labeled and sent to scrap area. The dust from the whole room from ceiling to walls progressing to downwards including pallets, trolleys SOP stand accessories box weighing balance air handling unit (AHU) supply/return grilles switchboards is removed using the vacuum cleaner and wiped with vacuum cleaner. The waste material is then collected, put into suitable poly bags, tied up, labeled and then sent to scrap area. All item present in room are mopped with dry duster and then with wet duster using disinfectant solution**.** The drain points are cleaned and sufficient volume of disinfectant is poured. The whole cleaning activity should be recorded in the cleaning record log book and specific log book of item present in the room.

Evaluation of cleaning

Visual Cleaning Test:-

All parts of equipment which are in direct contact and non-contact with products should visually check and verified for cleanliness.

Spiking test:-

This test verifies the cleaning of equipment visibly, there should be no residue. A diluted series of the worst case are made in volatile solvent and applied on surface of test equipment, which is similar to the sample surface (e.g. 25 cm^2). The active ingredient quantity should be distributed uniformly on surface of test equipment; the test should be performed by using different concentrations and also mimicking the same test conditions using approximate volume.

The solvents are then evaporated to determine the visual limit of detection by comparing with the test surfaces of equipment. But this limit can be affected by light intensity, surface characteristics, and method handling by operators' or operator itself. Therefore all the condition related to the test should properly match with the validation studies conditions. This test is not performed for the materials, which are Generally Recognized as Safe (GRAS).

Sampling Techniques

Sampling sites was selected based on the difficult clean geometries of the equipment and these locations are inaccessible their inaccessibility makes them difficult to clean therefore, before choosing for sampling sites one must be conscious in selecting the desired sampling locations. Laboratory is characterized into hot spots and critical sites. Hot spot is the location that is likely to become dirty during the manufacturing process and it is difficult to clean. Critical sites are those locations if remain dirty will certainly show disproportionate level of contamination to the next exhibit.

There are several types of sampling in the program of cleaning validation:-

Swab Sampling

It usually requires materials which are absorptive & to physically wipe the surface and recover the analyte. Because the need to physically wipe the surface was the preferred method that is readily accessible to human hand or arm.

Rinse Sampling

Rinse sampling does not employ mechanical action on the surface and the sample is collected as a final rinse or rinse applied specifically for collecting a validation sample.

Placebo Sampling

Placebo is recognized as both potential cleaning techniques and potential sampling techniques. Placebo material comprises of all typical excipients but not the active ingredient. And the placebo batches were passed through a same line so that it will have possibility to scrub of the clean system. The principle involved in placebo is that it is passed through the same pathway as the product therefore; it will have the possibility to scrub off residual product.

Direct Sampling

It is done by using FTIR or photoelectron emission techniques. By employing these techniques, specific spectra obtained from residue remaining on the surface will directly measure the quality of the surface. The advantage of using these techniques is that sampling and analysis will be taking place in one step and there will be no real loss of sampling system. Whereas in swab sampling direct analysis of the surface is limited to the area that are accessible for inspection.

Airborne microbial sampling

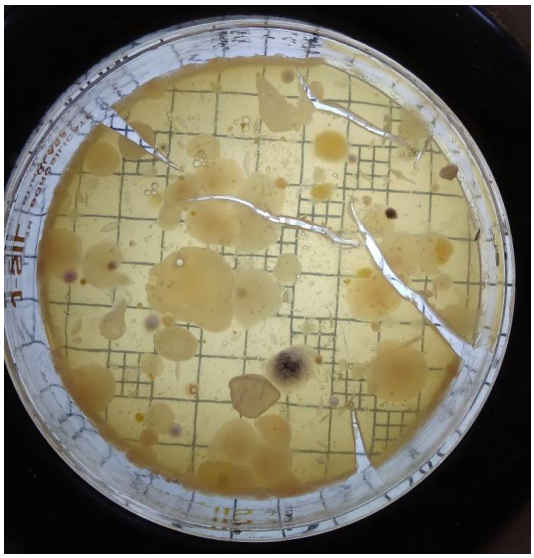
The microorganisms present in air will be count by Petri dish method, a sterilized Petri dish with identification number containing suitable nutrient medium will be used. The various locations are selected for sampling or placing the Petri dish.

The sampling time is 20 mints at every location. After completion of sampling plates will be placed in incubator maintain inverted to prevent condensation drop for period of 18-24 hrs at $35^{0.}$. After incubation number of colonies on each plate will count by digital colony counter.

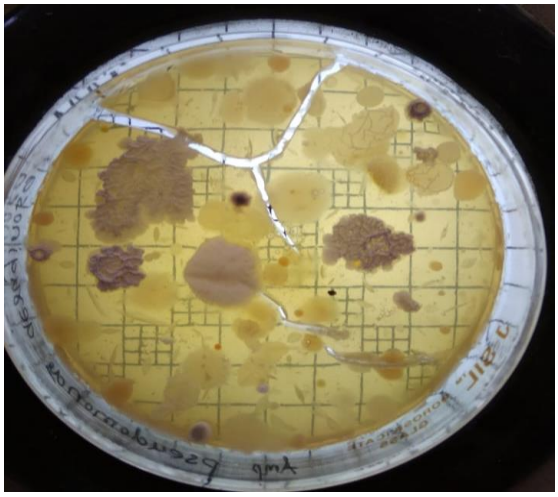
Acceptance criteria

The acceptance criteria as per guidelines of company is maximum number of colony per square foot should not exceed 100.

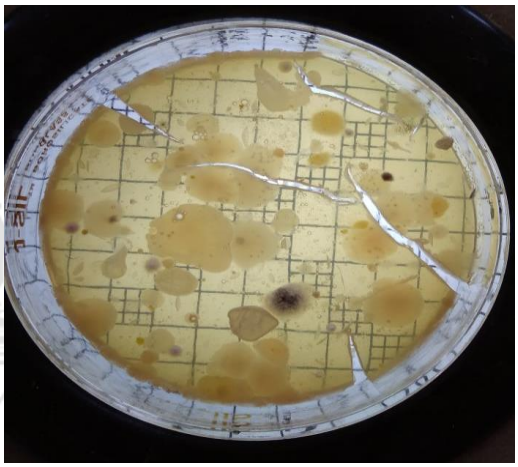
Location of Petri Plates



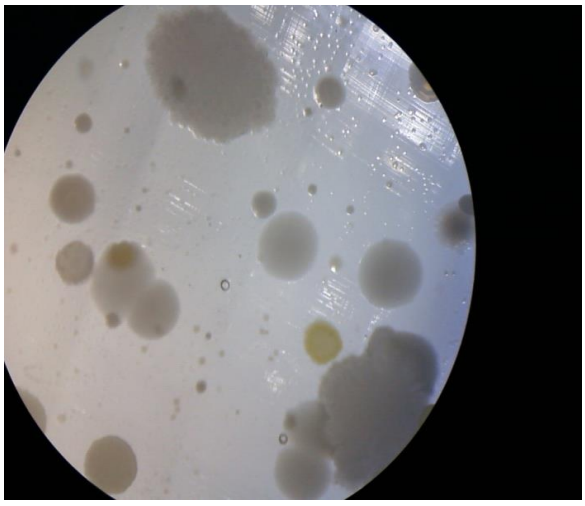
Pharmacology Lab Sampling and Counting **PLATE NO. 1**



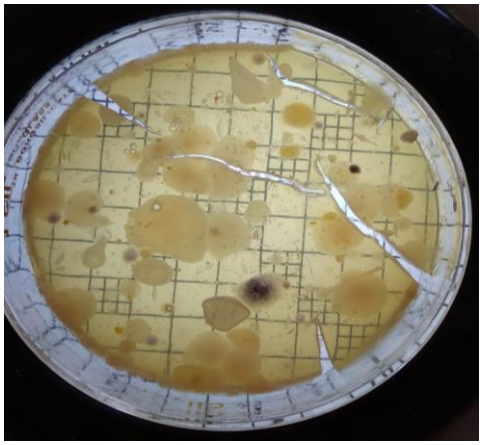
Microbiology Lab Sampling and Counting **PLATE NO. 2**



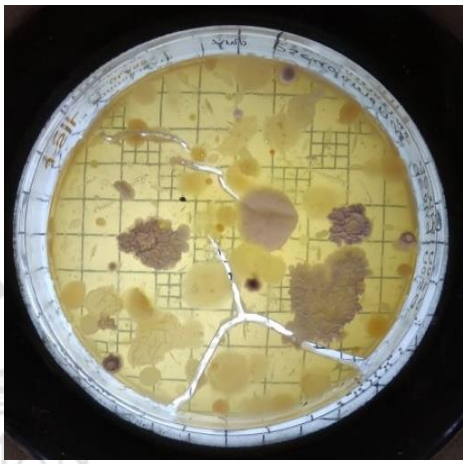
Pharmaceutics Lab Sampling and Counting **PLATE NO. 3**



Pharmacognosy Lab Sampling and Counting **PLATE NO. 4**

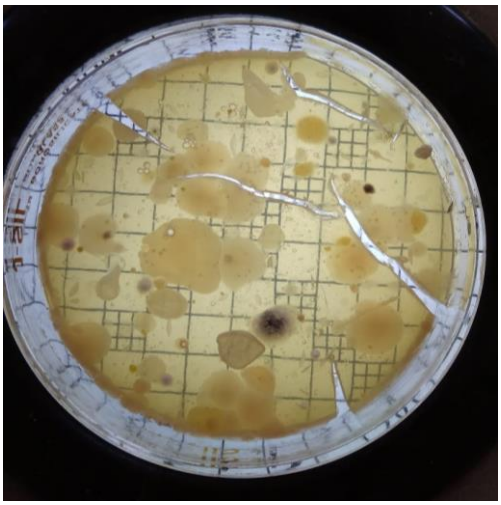


Student Toilet Lab Sampling and Counting PLATE NO. 5



Pharmaceutical Chemistry Lab PLATE NO. 6

Sampling and Counting



Student Toilet Lab Sampling and Counting PLATE NO. 7

STANDERD OPERATING PROCEDURE FOR CLEANING

TRAINING PROGRAMME FOR LAB PEON REGARDING TO CLEANING PROCEDURE

A training program is conducted for lab peons and other peons to train them to implement newly implemented cleaning methods this program includes following,

1. Filling and maintaining cleaning records daily

2. Necessary precaution need to be taken during cleaning.

3. How to use SOP for cleaning.

4. Correct methods of cleaning.

5. Combination use of disinfectants

6. Adherence to cleaning method designed by management.

7. Importance of maintaining hygiene and cleanliness.

8. Video demonstration of ideal cleaning procedure

Calculation

Colony Forming Units

Definition:-

Calculate the no. of bacteria (CFU) per milliliter or gram of sample by dividing the no of colonies by the dilution factor multiplied by the amount of specimen added to agar plate.

Formula:-

$$C = \frac{n}{s} \times d$$

Where,

C = Concentration, CFU/ml

n = No. Of Colonies

S = Volume transfer to the plate

d = Dilution blank factor

CALCULATION:-

- Before / After Using Of Cleaning Agents Counting Of CFU For Plate No. 1

Formula:-

Before

$$C = \frac{n}{s} \times d$$

$$C = \frac{76}{10 \times 1}$$

$C = 7.6 \times 10^1$ CFU/ml

After

$$C = \frac{n}{s} \times d$$

$$C = \frac{32}{10 \times 1}$$

$C = 3.2 \times 10^1$ CFU/ml

- Before / After Using Of Cleaning Agents Counting Of CFU For Plate No. 2

Formula:-

Before

$$C = \frac{n}{s} \times d$$

$$C = \frac{80}{10 \times 1}$$

$C = 8 \times 10^1$ CFU/ml

After

$$C = \frac{n}{s} \times d$$

$$C = \frac{34}{10 \times 1}$$

$C = 3.4 \times 10^1$ CFU/ml

- Before / After Using Of Cleaning Agents Counting Of CFU For Plate No. 3

Formula:-

Before

$$C = \frac{n}{s} \times d$$

After

$$C = \frac{n}{s} \times d$$

$$C = \frac{120}{10 \times 1}$$

$C = 12 \times 10^1$ CFU/ml

$$C = \frac{76}{10 \times 1}$$

$C = 7.6 \times 10^1$ CFU/ml

- Before / After Using Of Cleaning Agents Counting Of CFU For Plate No. 4

Formula:-

Before

$$C = \frac{n}{s} \times d$$

$$C = \frac{126}{10 \times 1}$$

$C = 12.6 \times 10^1$ CFU/ml

After

$$C = \frac{n}{s} \times d$$

$$C = \frac{76}{10 \times 1}$$

$C = 7.6 \times 10^1$ CFU/ml

- Before / After Using Of Cleaning Agents Counting Of CFU For Plate No. 5

Formula:-

Before

$$C = \frac{n}{s} \times d$$

$$C = \frac{156}{10 \times 1}$$

$C = 15.6 \times 10^1$ CFU/ml

After

$$C = \frac{n}{s} \times d$$

$$C = \frac{89}{10 \times 1}$$

$C = 8.9 \times 10^1$ CFU/ml

- Before / After Using Of Cleaning Agents Counting Of CFU For Plate No. 6

Formula:-

Before

$$C = \frac{n}{s} \times d$$

After

$$C = \frac{n}{s} \times d$$

$$C = \frac{85}{10 \times 1}$$

$$C = \frac{32}{10 \times 1}$$

$C = 8.5 \times 10^1$ CFU/ml

$C = 3.2 \times 10^1$ CFU/ml

- Before / After Using Of Cleaning Agents Counting Of CFU For Plate No. 7

Formula:-

Before

$$C = \frac{n}{s} \times d$$

$$C = \frac{176}{10 \times 1}$$

$C = 17.6 \times 10^1$ CFU/ml

After

$$C = \frac{n}{s} \times d$$

$$C = \frac{89}{10 \times 1}$$

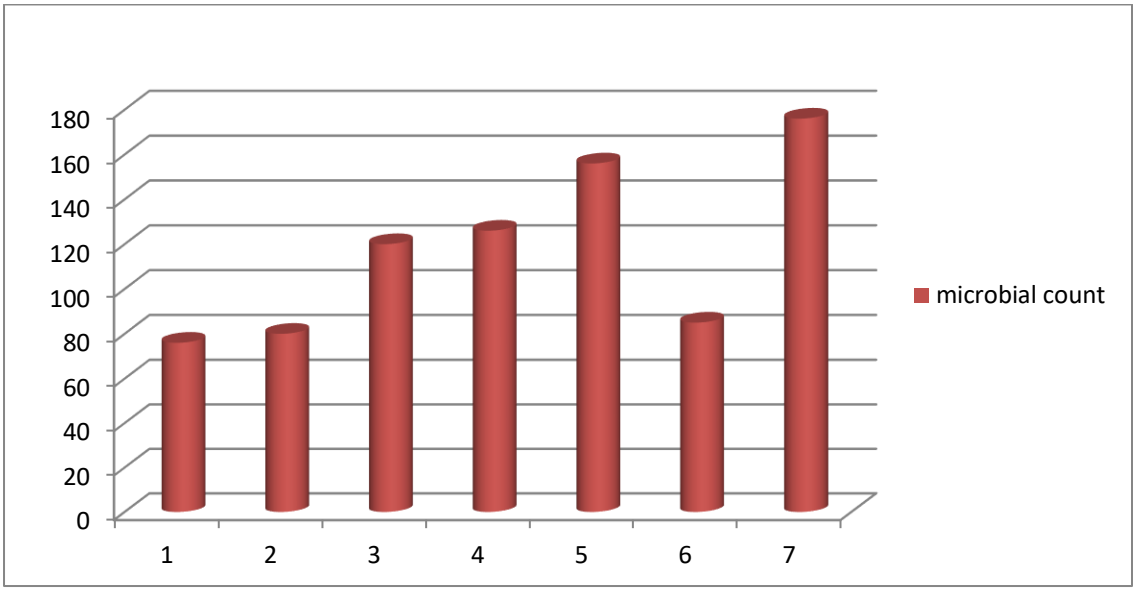
$C = 8.9 \times 10^1$ CFU/ml

Observation:-

Sr. No.	Location Of Plate	Colony Counting		CFU/ml	
		Before	After	Before	After
1	Pharmacology Lab.	76	32	$C = 7.6 \times 10^1$ CFU/ml	$C = 3.2 \times 10^1$ CFU/ml
2	Microbiology Lab.	80	34	$C = 8 \times 10^1$ CFU/ml	$C = 3.4 \times 10^1$ CFU/ml
3	Pharmaceutics Lab.	120	76	$C = 12 \times 10^1$ CFU/ml	$C = 7.6 \times 10^1$ CFU/ml
4	Pharmacognosy Lab.	126	76	$C = 12.6 \times 10^1$ CFU/ml	$C = 7.6 \times 10^1$ CFU/ml
5	Student Toilet	156	89	$C = 15.6 \times 10^1$ CFU/ml	$C = 8.9 \times 10^1$ CFU/ml
6	Pharmaceutical Chemistry (phd.) Lab	85	32	$C = 8.5 \times 10^1$ CFU/ml	$C = 3.2 \times 10^1$ CFU/ml
7	Staff Toilet	176	89	$C = 17.6 \times 10^1$ CFU/ml	$C = 8.9 \times 10^1$ CFU/ml

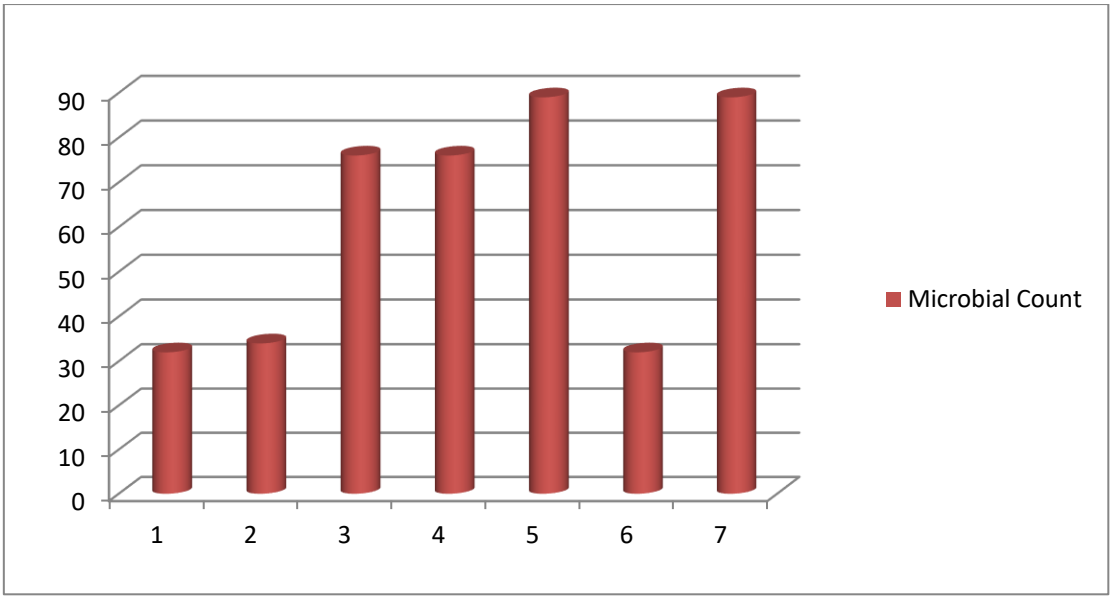
Graphical Representation: - Before Cleaning

Plate N o	Microbial Count (Before)
1	76
2	80
3	120
4	126
5	156
6	85
7	176



Graphical Representation: - After Cleaning

Plate N o	Microbial Count(After)
1	32
2	34
3	76
4	76
5	89
6	32
7	89



Revalidation Criteria:-

A close view is placed to ensure that some changes can affect the whole cleaning process are identified and recorded. The changes are reviewed; if they have significant effect then the change proposal is made through the change control procedure, which is documented and authorized. If the change is minor or it has no direct effect on result of the performed practical only by the documentation Revalidation is necessary when;

1. The product has less solubility than the pre- considered worst-case product.

2. The new drug has low potency than the pre- considered worst case product.

3. The equipment is change or there is any major modification, which can affect the contact surface area.

4. The cleaning agent or its concentration is changed.

5. The cleaning procedure is changed.

6. The procedure gets failed during routine monitoring.

Validation Report:-

The validation report is then prepared which contains the result, conclusion and secured approval of the study.

The validation report includes the following:

1. The references/summary of the method used for cleaning, sample and test.

2. The analytical, physical and other observations of test result or reference.

3. The final conclusion with respect to acceptability of the results, and the status of the procedure(s) being validated.

4. If there is any a recommendation given on the basis of the result or information obtained during the study for example revalidation of process.

5. Approval of conclusion.

6. If there is any deviation occurred then protocol is reviewed**.**

RESULT:-

From the study of cleaning validation of different laboratories of Rajarambapu College of Pharmacy Kasegaon, we can found by the using of effective combination of disinfectant as Lysol: Dettol (2:4) and Phenyl: Dettol (2:4) and Phenyl: Lysol (2:2) reduces the growth of microorganisms.

DISCUSSION:-

The pharmaceutical laboratories should be free any contamination, cross contamination, it would be safe for the performing practicals and gives better result. With the help of cleaning validation any laboratory of Rajarambapu college Of Pharmacy, Kasegaon can achieve high degree of assurance regarding the cleaning, with this we can minimize any kind of contamination or cross- contamination which is may be any residue of previous practicals performing, substance of machine or any microbial contaminations. For better performance in the practical need to cleaning of the laboratory. While the regarding health of the students in RCP, Kasegaon cleanliness is necessary.

There are different labs having different microbial count & the highest microbes are present in toilets .So need to cleaning with different chemicals or cleaning agents. By the using different chemicals or different concentration of cleaning agent cleaning should be proceed as per SOP's of cleaning validation.

REFERENCES:-

1. Manohar A. Potdar , " Pharmaceutical Quality Assurance" , Nirali Prakashan , third Edition , October 2013, Page No. 8.22
2. Dr. Chandrakant Kokare , "Pharmaceutical Microbiology Principle & Application" , Nirali Prakashan , Tenth Edition , July 2015 , Page No. 5.16 – 5.19
3. (Late)R.Ananthanarayan , CK Jayram Pnikar , "Textbook Of Microbiology" , Universities Press , Seventh Edition , 2005 , Page No. 34,44,124
4. A REVIEW ARTICLE ON CLEANING VALIDATIOND. Narayana Murthy and K. Chitra, Sri Ramachandra College of Pharmacy, Sri Ramachandra University, Chennai-600 116, Tamil Nadu, India
5. Y. Anjaneyulu , R. Marayya , "Quality Assurance & Quality Management In Pharmaceutical Industry" , PharmaMed Press , Second Edition , 2003 , Page No. 34,125,146
6. Dr. K. P. Bhusari , Dr. U. D. Shivhare , D.C.Goupale , "Pharmaceutical Quality Assurance & Management " , PharmaMed Press , 1st edition , 2013
7. A REVIEW ON CLEANING VALIDATION IN PHARMACEUTICAL INDUSTRY , Raj Pal Govind *, Arya Rajeshwar Kamal Kant, Joshi Tanuj, Bisht Dheeraj , Department of pharmaceutical sciences Kumaun University campus Bhimtal Nainital, India