COATINGS BIOCIDES

Practices for Preventing Microbial Contamination in Manufacturing:

Cleaning, Sanitization and Maintenance

ROHM AND HAAS

imagine the possibilities™

Bulk storage

Bulk delivery

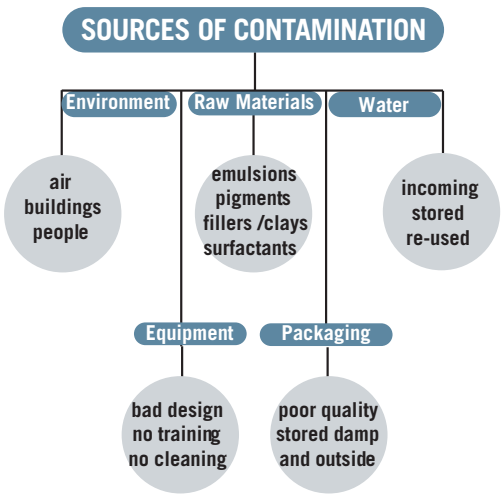
Filling line

Mix tank

THE CHALLENGE

The ever increasing environmental demands on raw materials and finished products have led to the development of new low VOC (Volatile Organic Compounds) formulations. These products, while being more environmentally friendly, are also more friendly to micro-organisms. At the same time raw material manufacturers, such as emulsion polymer suppliers, have been reducing the amount of free monomers in their products. These free monomers imparted a degree of biocidal effect to both the polymer and the finished product. The combined effect is that these low-VOC products are more readily susceptible to microbial attack during manufacture, during storage, and in the final container. (see figure 1).

Figure 1



The establishment of Good Manufacturing Practices(GMP) with respect to plant cleaning and sanitization needs commitment from management. Cleaning and sanitizing practices should be programmed like preventative maintenance and incorporated into your quality management system. Indeed, many companies have now written such procedures into their Quality Management Systems.

The aim of this booklet is to provide suggested practices with respect to preventing microbial contamination in manufacturing.

AREAS OF CONCERN

The following areas are the most at risk and, therefore, should be addressed before starting the cleaning and sanitization procedures.

Plant HouseKeeping

- Make an operator responsible for the tidiness of a work area.
- Mend broken windows and doors and seal unwanted openings, thus preventing air currents, which can introduce and spread bacterial and fungal spores.
- Control dust from powdered raw materials. Install U-type make-up air vents on storage tanks. Keep hatch covers closed.
- Clean walls and ceilings in wet humid places and consider using a fungicidal paint.
- Keep floors clean and dry, and remove spills immediately.
- Floors should allow proper drainage.
- Throw away any trash e.g. cleaning rags, paper towels etc.
- Cleaning equipment such as buckets, mops and hoses should be drained and stored dry between uses.
- Store empty hoses on racks that allow for complete drainage.

Hydroblasting equipment

Lab testing

Checking production batch

Maintaining clean process equipment

Equipment and Design
(see figures 2 and 3)

- Vessels should be constructed of smooth, polished metal, preferably 316 L stainless steel, not porous materials such as fiberglass reinforced plastic. Storage tanks composed of crosslinked polyethylene are preferable to fiberglass reinforced plastic tanks.
- Equipment should be easy to clean back to bare surfaces to prevent the formation of build-ups and biofilms. Many biocides and sanitizing agents are not able to penetrate polymer films and biofilms. (see figure 2)
- Equipment should be able to tolerate the cleaning and sanitization chemicals used.
- Design the plant to eliminate "Dead Spots", especially in pipe work where microorganisms can accumulate, breed and then infect fresh product. (see figure 3)
- Pipe-runs should be short, straight and sloped, i.e. >1% for long runs, >5% where possible for good drainage. Pipe-runs with wide angle sweeps will facilitate pigging.
- "Pigs" should be used to prevent build-ups inside pipework. Disposable pigs are recommended and should be discarded after use.
- Mixing vessels should be covered to prevent environmental contamination.
- Filling lines and filling heads should be cleaned and sanitized on a regular schedule to prevent cross contamination.
- "Splash-Zones" in vessels should be cleaned and sanitized regularly.
- Design and install hose racks that allow hoses to drain completely.
- Closed systems should have inspection points where build-ups can be easily monitored.
- Pumps should be checked, cleaned and sanitized regularly. Choose hygienic pumps, e.g. those with vertical inlet and outlet.
- Inlet manifolds should be cleaned and sanitized routinely. It is not advisable to pump in and out using the same manifold, so as to avoid any cross-contamination.
- Valves should be cleaned and sanitized regularly.
- Straining and filtering apparatus should be cleaned and sanitized regularly. Use disposable mesh filters when possible.
- Equipment used to transport finished or partly finished product around the plant should be regularly cleaned and sanitized.
- Keep transfer lines fully flooded or well rinsed and drained between uses.

Figure 2

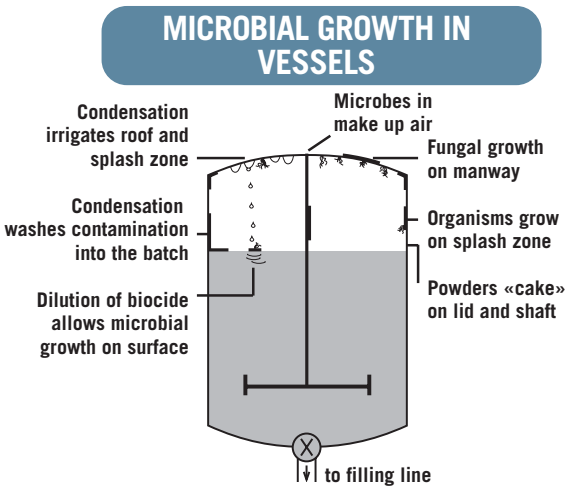


Figure 3

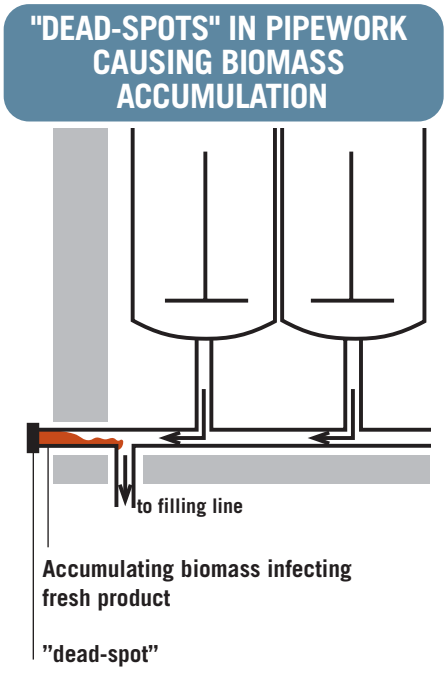


Figure 4[1]

EXAMPLES OF MICROORGANISM LEVELS THAT CAN BE FOUND IN RAW MATERILS

Raw Material Type	cfu / g *
EMULSION	
Acrylics	5.3×10^5
Vinyl Acetate-Copolymer	1.0×10^7
Vinyl Acetate-Butyl-Acrylate Copolymer	1.0×10^4
PIGMENTS	
Titanium dioxide	1.0×10^2
Chromium, powder	6.1×10^2
Copper phthalcyamine paste	1.5×10^3
FILLERS	
Calciumcarbonate	1.5×10^8
Magnesium-aluminium-silicate	1.3×10^7
China Clay	1.0×10^8
Barium sulphate	1.0×10^2
ADDITIVES	
Casein	3.4×10^6
Carboxy methyl cellulose	7.0×10^8
Hydroxy methyl cellulose	2.9×10^4
Process water	2.8×10^5
Softened water	1.0×10^4
Tap water	1.0×10^3

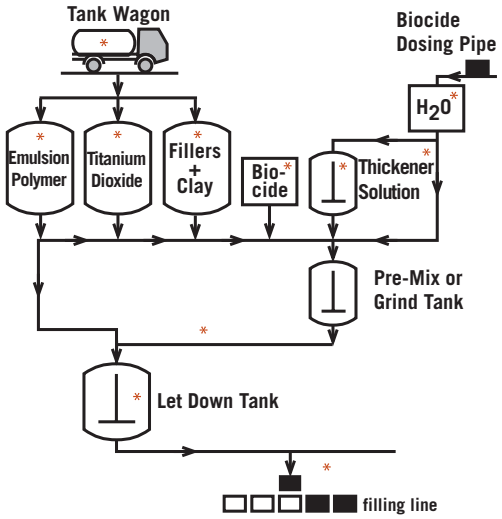
All numbers are mean values.

[1] Source: H. Brill. Mikrobielle Material-zerstörung und Materialschutz. Gustav Fischer Verlag Jena 1995.

* Colony forming units per grams

Figure 5

SIMPLIFIED DIAGRAM SHOWING HIGH RISK AREAS * IN A PAINT-MAKING PLANT



Raw Materials and Finished Products (see figures 4 and 5)

- Establish good stock rotation procedures, "first in, first out".
- Store all raw materials inside if at all possible. Re-seal any open sacks and protect from temperature extremes.
- Identify susceptible raw materials and set microbiological specifications with suppliers.
- Store all finished product containers inside in a clean, dry and dust-free environment. Shrink wrapping helps minimize the risk of microbial contamination.
- Recycled wash water should be turned over quickly and dosed with biocide, if it is held for more than a few hours.
- Check raw materials that are susceptible to microbial contamination and monitor during storage.
- Ideally, bulk storage tanks should be equipped with an agitator and with a humidification system to help prevent skinning. Ensure underside of agitator is cleaned and sanitized regularly.
- Do not back flush during cleaning of bulk tank lines into bulk storage tanks. Disconnect and flush with water and/or dry before reconnecting to storage tanks.
- Design a bulk storage tank cleaning, sanitizing and rinsing program. Depending on the raw material, this procedure may need to be done every 12 to 36 months.
- Ambient air introduced during the filling of bulk tanks should be avoided. Air filters or U-type make up air vents should be fitted and regularly cleaned and maintained.
- Minimizing the head-space in bulk tanks reduces the risk of condensation and hence, microbial contamination.
- Pre-mixes of raw materials such as thickener solutions need an addition of a biocide, even if they are only going to be stored for a few hours.
- Fillers and Clays: Natural products like these are often contaminated with either bacterial or fungal spores or both when in powder form. These spores will then germinate in an aqueous environment. In slurry form, a biocide is required to protect the product.
- Pigments are supplied as powders, as a paste/ dispersion or as a slurry. Their microbiological condition should be regularly monitored upon receipt and during storage.
- Surfactants/ Defoamers (antifoams): These water-based products are easy to contaminate with microorganisms, if they are not well preserved.
- Check process water on a routine basis (not less than quarterly) to ensure water is clean.
- Install a process water sanitization system if water does not meet quality specifications. If using UV, monitor on a routine basis to ensure operability or install a failure alarm.

THE CLEANING AND SANITIZATION PROCEDURE

Having established the quality and microbiological condition of the raw materials and the cleanliness of the manufacturing equipment, consideration now needs to be given to the actual cleaning and sanitization program itself. The more frequent the cleaning, the less rigorous or frequent the sanitization procedure needs to be.

The cleaning and sanitization procedure should be regarded as an on-going program to be performed regularly and not only for when problems have occurred.

Cleaning only removes the organic and inorganic debris. Sanitization, however, eradicates microbial contamination. The two terms are not synonymous and should not be confused.

Cleaning should always come before sanitization, as it is not possible to sanitize a dirty plant.

Soils may be removed by chemical or mechanical methods. A cleaning treatment may include water, surfactants, and mild acids to remove organic soils, and/or alkalines to remove polymers and inorganic/mineral deposits. Heavy buildup may require more aggressive means, such as pressurized water, sand blasting or manual scrubbing, scraping and brushing. Use 'pigs' to clean transfer lines.

Cleaning alone is not effective in penetrating or eliminating biofilms. However, frequent cleaning can prevent biofilms from becoming established.

There are many ways of sanitizing a plant.

An important point about any sanitization program is not just to consider the specific treatment used but also the contact time. The longer the contact time, the more effective the treatment will be.

- **Steam:** The circulation should be for at least 30 minutes at 90 to 100°C throughout the entire system. It can be difficult to monitor its effectiveness throughout the entire system. If any part of the system does not reach the required temperature and time, this practice is not effective.
- **Hot water:** This is extremely effective if 82°C and a minimum of 30 minutes contact time are achieved throughout the entire system.

  However, water is not a good wetting agent and dissolver of build-ups and, as a result, needs the addition of other chemicals, such as surfactants.
- **Chemical Disinfectants:** There are two main types of disinfectants, oxidizing and non-oxidizing. These compounds are fast-acting and broad spectrum in activity (see Table 1 below for more details).

Table 1. Chemical Disinfectants*

CHEMICAL DISINFECTANT	TYPICAL TREATMENT LEVELS (%ACTIVE INGREDIENT)	CONTACT TIME
Oxidizing Disinfectants:		
Sodium Hypochlorite	0.01 to 0.02%	30 minutes
Peracetic Acid	0.01 to 0.2%	5 minutes
Hydrogen Peroxide	0.05 to 0.1%	30 minutes
Non-Oxidizing Disinfectants:		
Quaternary Ammonium Chloride	0.02 to 0.04%	10 minutes
DBNPA	0.02 to 0.04%	240 minutes

** Be sure to follow the label recommendations and the supplier's MSDS to ensure proper use and handling. Note : these are guidelines on treatment levels and contact time, which should be verified and, if need be, adjusted based on field experience.*

- **Hot Caustic:** Extremely effective, but presents a safety risk to personnel and is corrosive to some equipment. Partially dissolved sludge may foul lines, and waste products may be difficult to discard.

After cleaning and sanitization

Cleaned and sanitized equipment should be drained dry and any open ends covered and labeled as clean to prevent microbial recontamination. In addition, the following steps are suggested:

- If not completely dry, equipment should be used within one hour or re-sanitized prior to next use
- Reactors/tanks should have manways and openings closed
- Flexible hosing should be dedicated to cleaning and sanitization and stored to facilitate draining and drying between uses.
- Filter pots/piping should not be left open to the atmosphere
- Conduct microbiological spot checks to confirm the effectiveness of the sanitization process.

** microbial audits include a systematic sampling and analysis of all plant areas that are prone to microbial contamination*

MICROBIOLOGICAL MONITORING

Microbiological audits* are an extremely useful tool for monitoring the effectiveness of your cleaning and sanitization program. Contaminated areas or product can be identified and remedial action taken to prevent the outbreak of a major problem. This helps avoid the risk of costly product recalls and minimizes production downtime.

Perform regular microbiological checks on susceptible raw materials, finished products, process water, and equipment on a monthly basis. Keep electronic logs of the results and choose a database that will give you the ability to perform trend analysis and pinpoint troublesome areas.

Discuss microbial susceptibility and preservative stability with your raw material suppliers and audit their control programs. Consider monitoring active biocide levels in raw materials and finished products. Develop documented "trigger points" and remedial active plans in response to confirmed positive test results.

Internal microbiological audits should only be performed by personnel, who have been properly trained in the aseptic techniques of sampling, where and when to take samples and how to package the samples for transport to the testing laboratory.

It is strongly recommended that external microbiological audits are also performed at least once a year by qualified Rohm and Haas personnel. Then areas, which may have been overlooked by plant personnel, can be identified for remediation.

For further information and assistance please contact your Rohm and Haas Company Account Manager.

GOOD MANUFACTURING PRACTICES FOR ROUTINE CLEANING AND SANITIZATION

Daily

- Tidy up, throw away trash.
- Keep your work area clean.
- Hang hoses vertically to allow liquid to drain away.
- Wash all mixing vessels with clean water and allow to drain properly.
- If re-using wash water, add a biocide as preservative.

Weekly

- Clean all vessels back to bare surfaces.
- Check filters and membranes for build-up.
- Apply sanitizing solution to all vessels.
- Rinse with clean water.
- Add a biocide to preserve to all rinse water to be stored.

Monthly

- Rinse entire system with biocide dosed, clean water.
- Check for build-up in bulk storage tanks.
- Conduct internal microbiological audit.

Quaterly or Semi-annually

- Empty, clean and sanitize all bulk storage tanks on a schedule which is based on microbiological monitoring findings.

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