

This article presents important considerations when designing thermal inactivation systems for bio-hazardous applications, and provides a comparison between properties of batch and continuous decontamination systems.

# Engineering and Design Considerations for Thermal Inactivation of Bio-Hazardous Waste Streams

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## Introduction

Downstream processing areas of pharmaceutical production facilities, research laboratories, and bio-containment laboratories are not often highlighted when looking at process solutions. This is often because this equipment is not in any contact with pharmaceutical products or visible in the research laboratory environment. Hidden among other utility-considered equipment, the effluent decontamination process equipment is a very important part of the facility activities required for daily operation and maintaining environmental safety. As environmental safety becomes more and more critical, it is extremely important to have a safe and economical means of treating process waste streams. Awareness of such systems design, purpose of use, requirements, and restrictions is important for upstream processes as well. It is important that architects, designers, engineers, and users take into consideration the designs of facility waste processing as part of the overall facility.

## Applications

Process areas that implement decontamination of bio-hazardous liquid and solid waste include bio-containment facilities, such as biotechnology research laboratories, infection control centers, animal and human pathology laboratories, military research, infection hospitals, university research laboratories, medical research facilities, pharmaceutical production plants, and even food processing plants.

Effluent streams can be sterilized by chemical or thermal means prior to discharge. The process can be a batch process or continuous process. Sterilization is a defined, validated process to inactivate all viable micro-organisms from the effluent prior to discharge. This renders the effluent safe to discharge to a sanitary sewer system. For effluent decontamination, validation may not be a correct term, but when used generally refers to a qualified process performance by microbial challenge testing.

There are two primary means to handle contaminated waste: 1. a batch process or 2. a continuous process. A thermal batch process consists of phases that include receiving effluent to a holding vessel, heating up to and holding at a specific exposure temperature in a decontamination vessel, and followed by cooling sequence, sampling phase, and discharge to drain after verified sample analysis results. A thermal continuous process configuration is a flow-through system that consists of a series of heating and cooling exchangers and a dedicated section for exposure at the specified temperature for a specific period

Figure 1. Continuous system.



of time. A continuous process can be sampled directly from the outflow or using parametric approach, as per described below in "Equipment Qualification."

Disinfection usually refers to a chemical process, generally recommended for small scale applications. Chemicals often used include sodium hypochlorite and peracetic acid, due to the broad-spectrum antimicrobial activity. The chemical is added and mixed at a known concentration directly into the effluent batch at a specific ratio, heated if required for more affect, and held for a specific retention time. The efficacy of chemical disinfection also can be verified by direct sampling and microbiological analysis.

The batch-based processes are usually referred to as conventional processes, such as kill tank systems. However, due to the waste-control demands of process and bio-containment facilities, continuous waste-reprocessing systems are becoming more suitable. The effectiveness and added safety of continuous processes have added value to the effluent waste process in modern facilities - *Figure 1 and Figure 2*.

## Batch Decontamination System

Basic operation of a batch decontamination system (kill tank) includes the following operational phases:

- receiving/filling
- heating
- decontamination
- cooling
- release/drainage or holding before release

Effluent is either pumped or gravity drained to a collecting vessel. When the vessel is full, the decontamination process can begin by heating up the vessel content by either direct steam injection, heating coils, or jacket heating. If effluent treatment is to be non-interrupting, at least two vessels or more are needed to enable continuous effluent collection ability, depending on the facility daily output and peak maximum flow. After reaching the decontamination set point, the decon-

tamination sequence is carried out by holding the effluent batch at specified temperature for a specified holding time. Typical decontamination temperatures vary between +121.1°C and +134°C and exposure times between 15 and 60 minutes. Maximum design parameters for a batch vessel are usually similar to a steam sterilizer (3 bar/+143°C). Higher design parameters often lead to a very expensive vessel structure. After decontamination sequence has elapsed, the tank is cooled down and de-pressurized by jacket cooling or cooling coils. In bio-hazardous applications, the decontaminated effluent may have to undergo sampling and analysis prior to release to environment (common drainage system). Analysis results take three to five days to be confirmed; therefore, the batch system may need additional vessel volume for batch holding prior to release.

## Continuous Decontamination System

For continuous decontamination systems, the effluent is collected to a collecting vessel in a similar way to batch systems. The continuous effluent processing system is started based on start and stop levels defined for the tank and measured by level transmitter or level switches. The decontamination process tunes up the process (heating and cooling) in a closed loop before the system goes online. Once the heating up period has elapsed, the process will advance to continuous processing mode, where effluent is taken directly from the collecting vessel and is heated, decontaminated, and cooled in a one way process until the stop level of the collecting vessel is reached. Decontamination takes place in a continuous flow through a dedicated pipe section after heating exchangers. There are temperature sensors in the beginning and at the end of the decontamination section, proving the decontamination exposure time and temperature during exposure time and the flow rate is constant. Continuous systems require significantly shorter exposure time due to high pressure and temperature conditions. Typical continuous decontamination temperatures vary between +150 and +165°C and exposure times between three and 10 seconds, depending on required lethality of the decontamination process. Heating media is plant steam. Increasing the decontamination process temperature decreases exposure time requirement exponentially. This applies to sterilization in general. Therefore, exposure times for continuous decontamination systems are significantly shorter, and usually defined in seconds rather than in minutes. After the decontamination section, the effluent flow is directed through cooling heat exchangers prior to discharge. The decontamination process performance qualification is verified during commissioning and due to the type of process and ideal process measurement conditions (turbulent flow, small momentary processing volume through the decontamination section) the continuous process can rely more on parametric control and replication of qualified process conditions.

## Process and Equipment Design

The following criteria directly affect the determination of the applicable type of decontamination equipment:



Figure 2. Batch decontamination system.

- bio-safety level of the application by environmental national and local laws, regulations, directives, and guidelines
- daily maximum quantity of effluent/peak volume of effluent vs. available technical space
- composition of effluent
- safety and redundancy requirements
- availability of utilities
- qualification requirements

Bio-safety levels (e.g., BSL1 to 4, CL1 to 4, and BL-1 to 4) define the required level of bio-containment depending on the biological organisms present. Levels 1 and 2 stand for minimal or moderate risks and levels 3 and 4 have high risk of infectious diseases and contamination.

Due to low risk of contamination, level 1 and 2 equipments are typically placed in general utility areas with the ability to use liquid disinfectants in case of a leak situation or to service the decontamination equipment. Access to the control system should be controlled by sufficient password protection and operating level limitations. In case of possible future upgrade from level 2 to level 3, a proper bio-containment room design is recommended for decontamination equipment, as well as considering the type of equipment to fulfill future requirements. In such situations, the design should allow for upgrading the existing system easily without considerable re-work of the space or equipment. In such cases, it is recommended to qualify the selected system according to level 3 during this phase, and ensure that the selected system will meet the required demands of level 3 applications.

For higher containment applications, additional design and safety considerations should be followed. The environment and mechanical space access to equipment at level 3 and especially level 4 containment areas is very limited so automatic and self-diagnostic operation with local and remote control, alarm functions, BMS (BAS) monitoring, and “hand-shake” signals communicating system status upstream are required. Strict control system access protection is also very important. In case of an emergency situation, the user should be able to carefully evaluate the equipment status and carry out all required safety measures from outside prior to entering the equipment room. Room decontamination from outside the space using a gaseous process (such as vaporized hydrogen peroxide) fed through specific wall ports should be arranged as well as using applicable liquid sterilants for decontamination of leaks or spills. Service procedures and systems access must be designed accordingly and take into account the restrictions imposed by protective clothing and equipment access for servicing the equipment. Peripheral devices and precautions may not usually be considered part of the decontamination equipment, but should definitively be included in the design of the entire operation. Equipment qualification sets specific demands for the type of process and equipment within level 3 and 4 applications. These issues are studied in “Equipment Qualification.”

Daily maximum effluent quantity is an important factor in thermal sterilization systems. Batch processing of large daily effluent loads requires extensive storage and decontamination volumes as well as large technical spaces, which

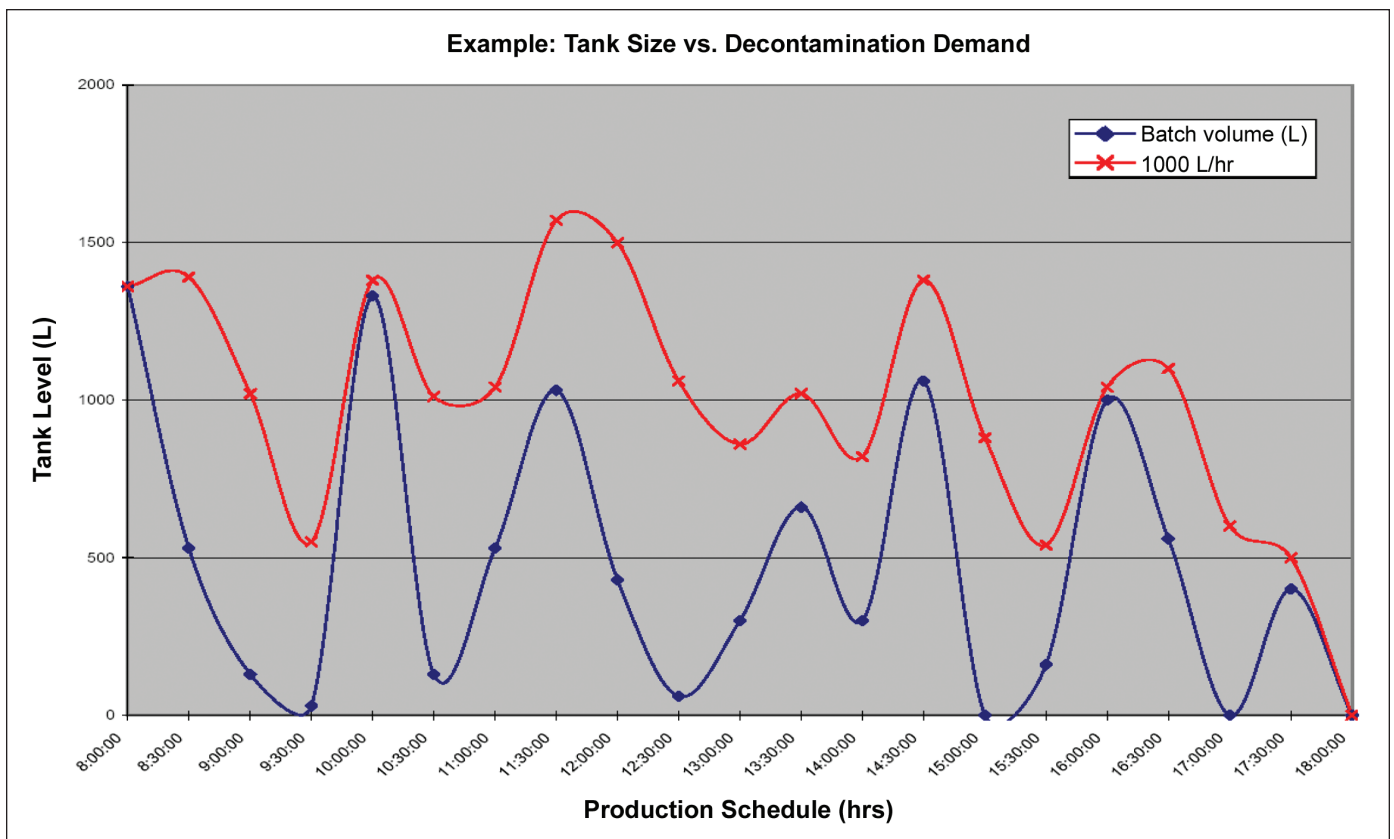


Figure 3. Daily effluent output evaluation example.



is a significant cost factor in new bio-containment facilities. Large batch systems are also often built and tested on site due to being limited by the size of the batch tank skids that can be transported. This makes batch systems more suited for small or single-point laboratory applications with small holding volumes such as table-top or under-counter installations. Continuous sterilization systems require a smaller footprint and can be manufactured and tested outside the facility - *Figure 3*. This makes continuous systems a more applicable solution for large capacities in terms of building and equipment capital costs, operational costs, and qualification.

The capacity vs. unit size efficacy for continuous systems is expanded by increasing only heat exchange surfaces, flow rates, and instrumentation sizes while batch systems require significant increasing of vessel sizes in addition to the need of having higher momentary capacity utility output needs. To be able to continuously receive effluent, it is required to have at least one vessel for collecting effluent and one for batch decontamination. In addition, there may be a requirement for another vessel for batch holding. Sample analysis requires four to five working days leading to equivalent holding time before the batch is permitted to be released to the common drainage system. For continuous systems, sampling can be performed directly from the outflow of decontaminated effluent, but a preferred method is described in "Equipment Qualification."

Table A shows a comparison between a batch and a continuous system. Decontamination capacity is 10,000 liters/day (during 10 hours of operation) for a BSL-3 application.

Stainless steel grade 316/316L is generally acceptable for contact surfaces, as well as PTFE based gasket material for their chemical and heat resistance. Following ASME BPE guidelines for materials of construction, components, and manufacturing methods ensures a reliable and functioning process system, as well as complying with the current GAMP guides even if decontamination systems are actually outside of the GMP (process contact) equipment scope.

For reliable service and consistent cycle results, process components and instruments should withstand steam sterilization and piping design should follow <3d "dead leg" rule where possible. Redundancy for critical process components is important in critical parts of the process (e.g., dual process pumps, dual barrier valves, dual critical temperature sensors, electrical heating for vent filtering, or dual vent filters). A single pass process minimizes any risk of cross-contamination between the contaminated effluent and decontaminated effluent. The design should avoid any return-loop connections between the effluent receiving area and the discharge area. Any shaft seals connecting to the contaminated side, such as pumps and tank agitators, should be avoided. Magnetic coupling is a leak-free solution for such applications. Temperature sensors are subject to frequent calibration and therefore should be installed in welded pockets that are not in contact with effluent. The number of connections should be minimized by applying preferably orbital welding techniques where technically possible, taking into consideration the service requirements of the components. The need for service is also

Capacity: 10 L <sup>3</sup> / 10 hrs	Continuous*	Batch**
Floor Space Requirement Est. (m <sup>2</sup> )	15	68
Steam Utility Size (kW)	77	355
Cooling Utility Size (kW)	53	163
Equipment Heat Loss to Environment (kWh)	18	88
Heating Energy Consumed (kWh)	790	1430
Cooling Energy Consumed (kWh)	530	815
Steam Consumption (kg) (Direct Steam System)	---	2356
*Continuous system with 1000 l/hr operation and 2000 L collecting tank **Batch system with receiving, sterilization and storage tanks		

Table A. Utility comparison table, calculation example.

reduced by minimizing the number of components and any moving or rotating parts. Mechanically polished or electro-polished finishes for contact surfaces promotes sterilization efficacy and minimizes possible fouling.

The effluent composition should be determined during the early stages of the process evaluation to accommodate design considerations for any chemical burden and prepare for possible handling of solids. High chlorine content combined with high processing temperature may require reinforcing process materials, but it is significantly less costly to limit chlorine content to a minimum and dilute in case of higher content.

Regardless of the processing method – batch or continuous – solid particles should be removed from the effluent stream and sterilized separately; even smaller particles than 10 mm in diameter. Larger particles such as carcass parts are usually sterilized and disposed of by using specific alkaline hydrolysis-based tissue digesting systems or incinerators. Solids can include any solid or slurry process residue such as carcass and tissue remains, proteins, agars, coagulated media (blood etc.), animal cage residues (bedding residue, food remains, feces, hair) among others. Direct steam injection



Figure 4. Solid waste sterilization test load.

tion sterilization in a relatively small volume breaks down solid mass and penetrates through the material, leading to a reliable sterilization result. The batch temperatures must be correctly measured from the coldest points and from the solids load to ensure a consistent result. Therefore, a smaller batch is preferred for solids sterilization.

Slurry and solid containing effluent leads to severe fouling of process surfaces and non-homogenous effluent batches can compromise process qualification integrity. Constant need for Clean-In-Place (CIP) of processing units is expensive and time-consuming, reducing the system uptime. Chemical pre-treatment of solids (e.g., proteins dissolution by alkaline or other) can be a very effective method to prevent fouling, especially for applications with egg proteins (vaccine manufacturing). If needed, correct pH level (7 to 9) should be adjusted for the effluent discharge prior to release to common drainage systems.

In addition to solids removal and alkaline dissolution of proteins, other fouling prevention methods include prevention of steam flashing during the sterilization process (superheated liquid processing), proper air removal, continuous mixing of slurry effluent in a collecting vessel, and keeping all process surfaces wetted at all times. Preventive actions such as adding water for dilution of effluent is recommended, but does not remove the need for the features mentioned above - *Figure 4 and Figure 5*.

Consistent availability of utilities is a common concern in any processing system. Thermal inactivation equipment requires house plant steam and/or an electrically heated system for thermal treatment of effluent, cooling water (closed loop or other type) for cooling down effluent prior to discharge, instrument air for pneumatic actuating instruments, and electricity for powering process components and the control system.

Batch processing equipment requires lower steam supply pressure (3 to 4 bar). The batch process temperatures are typically standard steam sterilizer cycle temperatures (+121.1 to +134°C), but apply long exposure times. Continuous systems require higher steam pressure (5 to 7 bar) for higher decontamination exposure temperatures (+130 to

+165°C) and respectively apply short exposure times, from seconds to a maximum of a few minutes. The general theory of exponential time/temperature correlation in moist heat sterilization processes defines the equivalency. Equal or higher kill efficiency when shortening exposure time is achieved by raising exposure temperature respectively. For example, 1.16 seconds at +150°C is equal to 15 minutes at +121.1°C.

Momentary consumption of steam, electricity, and cooling water of continuous systems is significantly lower to batch systems due to the use of ideal turbulent processing conditions, a superheated liquid process with relatively small amounts of continuous liquid treatment, and an effective heat recovery process. Batch systems also may require direct steam injection, which is not economical in larger applications due to the loss of plant water, residual condensate heating energy, and water treatment chemicals. This can be neglected in small point-of-use applications, but significantly raises annual operating costs in larger systems.

Cooling water and heating steam/electricity consumption can be significantly reduced by applying heat recovery to the continuous decontamination process. This means energy transfer from decontaminated hot effluent to the incoming contaminated cooler effluent prior to discharge. Specific attention should be given to the method of heat transfer. In a single pass solution with contaminated effluent on one side and decontaminated discharge effluent on the other, there is a severe risk of an undetectable cross-contamination. Heat transfer should be arranged so that the effluent streams are separated and pressure controlled where the decontaminated stream is always at higher pressure compared to the contaminated effluent. This reduces the heat transfer efficiency, but bio-safety measures are considered more important to energy savings when operational risks are analyzed.

Safety and redundancy evaluation by hazard analysis and process reliability and efficacy verification by process qualification also define the required characteristics when evaluating the decontamination system and equipment.

## Hazards Analysis

Hazards and risks analysis for decontamination systems should be carried out including the related systems, location, and surrounding environment. Minimizing the potential risks coming from the upstream process, laboratory, or other bio-containment activities should be taken into account before selecting the method of decontamination.

Minimize the quantity of effluent being discharged for decontamination. The less effluent produced, the easier the system is to design in terms of safety measures. Leave any unnecessary sources of liquid effluent outside the barrier. Leave out any unnecessary amounts of solids – anything that is harder to handle inside the barrier than outside, for example toilet waste. The more effluent produced, the more holding volume is required. Smaller volumes require smaller equipment and less room space. The smaller effluent stream also reduces the volume that could potentially leak. If a leak does occur, smaller spaces are easier to contain, clean, and decontaminate. High levels of solids can cause excessive foul-



Figure 5. After solid waste steam sterilization.

ing, operational problems, and critical downtime unless the decontamination process is designed properly to handle this type of waste.

Minimize the number of connections within the decontamination system – every connection is subject to leakage. Non-visible welds inside any structure should not be allowed in contact with the effluent. In case of a leak, detection in these areas is extremely hard or sometimes impossible. Pay attention to the type of instrumentation, process components, and installation as described below.

Continuous monitoring, self-diagnostics, full coverage alarming system, and repeatable qualification methodology are mandatory features for critical equipment. The end user must be able to safely control the process from outside, and even more important, to be aware of the system status at all times.

## Equipment Qualification

Equipment qualification methods and procedures should be required for any effluent processing system within bio-safety level 3 and 4 classified areas. Equipment qualification is based on sampling and laboratory analysis of the decontaminated batch before releasing the batch for discharge to the sewage system. The equipment performance can be qualified by using biological indicators with a specific population of a challenge micro-organism, typically *Geobacillus Stearothermophilus*. Depending on the bio-safety level of the application, a passing overkill result with a starting population of 106 CFU is generally required, and three consecutive successful tests are considered passing the biological challenge test.

Qualification of a batch process is simple and straight forward, but sampling from large volume vessels can create problems that may not be easily solved. This includes defining a valid and representative number of samples of a batch and a consistent qualification method for non-homogenous batches (including solid particles). Even when particle sizes are restricted, it may be difficult to prevent coagulation within the batch vessel. This leads to uncertainty of even temperature distribution due to pockets of large mass caused by solids coagulation or simply large size particles. Control over air pockets that can cause cold spots and temperature deviation during the batch decontamination are also difficult to prove by sensor monitoring or sampling even if no solids were present. Sterilization cycles are often run prior to servicing equipment. Simple processing equipment is an advantage for batch systems in terms of service cycle qualification, but larger scale systems face the same problem when testing the vessel for sterilization integrity.

In case of prions, specific time/temperature controlled batch inactivation cycles and alkaline-based inactivation cycles are applicable, as well as other processing methods that can be verified as compliant.

Service sterilization cycles of different isolated process sections (filters, tanks, strainers, etc.) are normally considered batch cycles and can be tested as such to ensure efficacy. For continuous decontamination systems, qualification of

the process should be based on biological challenge tests and sample analysis for equipment qualification purposes. Momentary processing volumes in continuous processes are minimal, homogenous, and with the aid of turbulent flow (for efficacy in temperature control and heat transfer) offer significant advantages when compared to batch processing conditions. Continuous processes sterilize a very small volume at any onetime and this allows redundant instruments to accurately monitor the process following a PAT type qualification scenario. This provides a significant advantage to batch processes that are challenging to monitor. A parametric release of the effluent is possible in continuous systems by ensuring the daily process parameters match those during qualification. Parametric release is a significant advantage over batch systems that may require sampling of each batch prior to discharge.

## Conclusion

Specific attention should be given to the design of the most suitable system for an effluent decontamination application. In addition to technical details comparison and overall applicability to the upstream process needs, the evaluation also should include long term lifecycle evaluation and functionality of the system in terms of qualification capabilities, daily operations, and required service activities. Batch processing systems are more suitable for smaller point-of-use and smaller volume applications, whereas continuous systems are more suitable in high containment applications with critical performance assurance and qualification requirements, as well as larger treatment volumes applications. Chemical processes (e.g., alkaline hydrolysis) are mainly used and recommended for carcass/tissue disposal and chemical disinfection methods for small-scale lab point-of-use.

For example, the NIH and CDC guidelines as well as European Union directives provide an excellent platform for definition of required precautions. However, a specific process design guideline for designing effluent decontamination process equipment could be a very useful addition for guidance to a safer environment and operation.

## References

1. Centers for Disease Control and Prevention (CDC). (2007). *Biosafety in Microbiological and Biomedical Laboratories* (5th ed.), HHS Pub. (CDC). Washington, DC: U.S. Government Printing Office.
2. *Industrial Moist Heat Sterilization*, Volume 57, (2003 Supplement), PDA Technical Monograph No. 1, (2002 Revision).
3. *Laboratory Biosafety Guidelines*, Public Health Agency of Canada (PHAC), Ottawa: Health Canada, Third Edition (2004).
4. *EN1620: Biotechnology – Large scale process and production – Plant Building According to the Degree of Hazard*.

5. *EN12740: Biotechnology – Laboratories for Research, Development and Analysis – Guidance for Handling, Inactivating and Testing of Waste.*

## About the Author



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