Validating the heat sealing process is thus critical both to comply with regulatory oversight and to be confident in the overall quality of the final product. Though there is some ambiguity in the industry as to the exact definition of validation, it is clear that all components of the sealing process that influence package integrity must be monitored, measured, and controlled. Moreover, equipment must perform the heat sealing function in a repeatable, invariable manner such that final product quality is consistent with predetermined standards. Typically, process control validation for heat sealing has dealt with three specific variables: dwell time, temperature, and sealing pressure.

This white paper reviews the relevant regulatory standard for medical heat sealing and discusses some of the important considerations that should go into implementing an effective validation process. After covering some of the design characteristics that ought to be prioritized when considering the abovementioned process variables, it goes on to make the case that process validation for medical heat sealing needs to include a broader range of parameters – including seal-area wrinkles, band breaks, and label applications – beyond the traditional three of time, temperature, and sealing pressure. Ultimately, for a piece of heat sealing equipment to be fully validated, total process control should encompass every step that affects the quality of the final product.

Introduction

Packaging plays a vital role in assuring the sterility of medical devices and instruments from manufacture to point of use. Applying effective heat seals to the package of terminally sterilized medical devices is arguably the most critical step to ensure the aseptic presentation of a product when it comes into contact with an end user or patient. No matter how robust the sterilization and disinfection process, if the packaging and seal closures of a medical pouch are compromised, there is significant risk of product contamination during shipping and storage that could pose serious danger to the end user.
Relevant Regulatory Standard: Navigating ISO 11607, Part 2

The relevant regulatory standard for validation of the heat sealing process for medical applications is ISO 11607, Part 2. It specifies the validation requirements for the forming, sealing, and assembly process for the packaging of terminally sterilized medical devices. As laid out in the standard, the objective of seal process validation is to document the sequence of events in which the process is established to produce effective seals that maintain sterility to the point of use and do so in a repeatable, reliable way. It is important to emphasize that the ultimate purpose of a packaging system for medical products is the maintenance of sterility: thus, the validation of packaging processes is crucial to guaranteeing the integrity of the final product.

ISO 11607 characterizes heat sealing as achievable with a bar sealer, impulse sealer, or a continuous feed sealer (rotary band sealer) and defines the critical parameters to create a proper seal as temperature, pressure, and dwell time. This white paper will focus on continuous sealing methods. The standard dictates that critical process parameters should be controlled, monitored, and documented and that, in the event that critical process parameters exceed predetermined tolerances, alarms, warning systems, or machine stops are initiated. An effective tool to meet this component of the standard is programmable logic controller (PLC), which can execute the alarms and machine stops and display immediate machine status. A PLC can also perform data logging that time stamps alarm history which is a benefit from a validation point of view. Additionally, the standard indicates that critical process instruments and sensors must be calibrated.

Furthermore, implementing process validation should include an Installation Qualification (IQ), Operational Qualification (OQ), and Performance Qualification (PQ), in that order. All steps taken to comply with ISO 11607 should be thoroughly documented and sampling plans to support validation should be statistically valid (See Appendix for further information on IQ, OQ, and PQ).

Prioritizing Design Features for Validatability

Given the demands of the validation process, there are some important design features that are optimal for validation that should be considered when specifying a piece of heat sealing equipment. As a general principle, equipment that includes instrumentation with maximum access, control and input from the critical process parameter areas (time, temperature, and pressure) will better facilitate validation.

For example, for measuring temperature, a heat sealer that monitors all heating bars individually rather than just one, affords enhanced process controls. For an additional level of security, temperature verification ports that are accessed externally can allow an operator to connect a calibrated temperature sensor to an individual port and verify temperature accuracy against the sealer’s temperature controller. Thermocouple sensors embedded within the heater cartridges themselves also assure a high degree of accuracy in temperature monitoring to sense deviation from set points.

Pressure readings, in the case of a continuous band sealer, are more accurate if pressure is delivered through air solenoids which can be calibrated and pneumatically controlled to provide consistent sealing pressure. This is in contrast to spring-based pressure which is difficult to measure accurately and not calibrated externally. Furthermore, each component in the sealing process needs to apply controlled pressure. Often times, only the heated sealing bars are measured and monitored limiting the effectiveness of the entire sealing process. Compression wheels and cooling bars are equally important to the overall sealing success of a band sealer and therefore must also be subject to process control.

Dwell times, reflected in speed measurements, should be measured and monitored with a PLC to offer a digital speed read out allowing real time speed monitoring.
Process Control Variables: Moving Beyond the Big Three

Historically, the three variables critical for medical heat sealing validation have been dwell time, pressure, and temperature. While crucial for an effective seal necessary to ensure sterility, it is possible to thoroughly validate a packaging process for these three parameters and still produce faulty seals that could ultimately imperil the safety of patients. There are other areas where process control could fail and threaten package integrity.

Any component of a sealing process is theoretically validatable. Process steps that can have negative effects on seal quality should receive heavy scrutiny and be incorporated into the validation process. A few salient examples include wrinkle detection, band breakage, and label application.

Wrinkles can occur throughout the seal even if temperature, pressure, and dwell time are all operating within accepted parameters. An effective validation tool for wrinkle detection can sense a wrinkled seal, trigger an alarm and cause the machine stop. If specified, an alarm can prompt a bag direction reversal and reject a bag back to the operator and then reverse back to normal operating direction once the defective bag has cleared the machine.

Likewise, band integrity is a critical factor not captured through traditional validation procedures. If all of the process variables are functioning within the effective ranges outlined in the Operational Qualification (see Appendix), but the sealer doesn’t have sealing bands installed, or they are worn, the creation of an adequate seal is not possible. A continuous sealer must monitor band integrity and be integrated into the PLC system to display current status and trigger alarms and stops when a band breaks or is missing.

Optical detection should be used for monitoring and ensuring accurate label application and the product being packaged matches the designation on the label. A camera can capture the image of a finished package and compare it to a pre-programmed image in which the correct label has been applied. Deviation from that standard image will result in a reject or alarm. These are some relatively prominent examples of process parameters that, though critical, fall out of the traditional scope of medical heat sealing validation. However, validation targets should not be limited only to what has been mentioned here. It is important to be able to engineer in validatability in a flexible manner, such that, for a given requirement, a process step can be easily incorporated into the validation procedure. Naturally, the demands of the market drive product development and today’s new requirement is tomorrow’s standard feature.
Appendix A: Installation Qualification, Operational Qualification, and Performance Qualification

Installation Qualification

The IQ verifies that heat sealing equipment is installed and calibrated correctly in order to ensure that the equipment can maintain critical process control and can perform consistently over time. During the IQ, critical process parameters are defined so that they can be controlled and monitored. This is also the stage in which alarms, machine stops, and warning systems are tested to trigger alerts when tolerances are exceeded. All instrumentation, sensors, displays, and controllers are certified as calibrated and written calibration procedures are developed along with preventative maintenance and cleaning schedules. Likewise, software systems are validated to ensure they function as intended.

Merely setting parameters is not sufficient for the IQ and all monitoring functions should show actual conditions. Gauges should show actual temperature, line pressure into the sealer, and have a method of reflecting real dwell time. Measuring instruments must be calibrated on a regular basis and documented to ensure constant adherence to set parameters.

Operational Qualification

The OQ verifies that the sealing process produces a sterile package at the extremes of set operational parameters. Qualifications are performed at upper and lower limits as part of this step to determine tolerances for error and the threshold for machine stops and alarms. For example, a particular package will have a range of settings for temperature, pressure and dwell time that will provide a good seal. A “good seal” should be intact with no channels, open areas, wrinkles, or creases. This range is specified to accommodate variability in environmental conditions within the production environment or the need to run different materials. The OQ identifies the upper and lower sealing parameter limits at which a good seal can be produced: a high speed/low temperature/low pressure value is set as “worst case” and a low speed/high temperature/high pressure value is set as “best case.” This process is conducted with the required seal strength and materials in mind.

Performance Qualification

The PQ is intended to assure that the sealing process will consistently produce sterile packages under the specified operating conditions set out in the OQ. Three production runs are conducted with different operators to evaluate if there is significant variation in output within the actual production environment. Typical variations are caused by changes in materials, operators, and environment and the PQ is designed to ensure that, given these difference, the machine still performs within tolerances. Appropriate operator training is important to guarantee consistency across different shifts and users. The PQ often uses real or simulated product and is the closest approximation to a genuine production run.

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