Auto-Sterility of Polymer Melts

Medical Technology. Industrial sterilization of a plastic for disposable medical applications in accordance with scientific criteria usually requires a costly, separate production step. Given the temperature and pressure conditions that obtain in the injection molding process, auto-sterile manufacturing of medical devices would be very efficient. New research results relating to validation of direct sterilization of the injection molding process are now available.

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Sterile, disposable medical products made from plastic are usually manufactured, assembled and packaged under standardized cleanroom conditions as a way of minimizing contamination. However, products made and packaged in this way do not satisfy the latest sterility requirements. The medical term "sterile" means free of bacteria and is an absolute term. In industry, though, a more precise definition, expressed as a probability, is applied, namely just 1 viable organism per 1 million parts [5]. Consequently, a manufactured and packaged product is only regarded as sterile if the aspects of polymer melt, the mold, part removal, and perhaps assembly, as well as packaging rule out the possibility of viable microorganisms on the product. This means that evidence of sterility cannot be adduced by making observations on individual manufactured products, but by validating the sterilization process. The Institute of Medical and Polymer Engineering at the Technical University of Munich is currently studying the auto-sterility of polymer melts in a project entitled Sterile Injection Molding (STIM) with a view to eventually establishing proof of sterile production.

One sterilization method which satisfies the sterility requirement consists in sterilizing the medical product after it has been packaged. Common industrial sterilization methods employ ethylene oxide (ETO) gas and gamma-radiation or electron-beams. Such sterilization systems are usually located not on the producer's premises, but rather in a separate sterilization facility away from the automated manufacturing process. Reasons for this separation include the enormous amount of equipment needed (e.g. shielding of ^{60}CO sources for gamma sterilization) and government regulations. Although this approach has proved adequate for modern disposable medical products, there are commercial and material disadvantages to separating production from sterilization [3]. Current sterilization methods cannot be integrated into the production process due to the sterilization times and space required. As a result, resort is made to batch processing. Along with the usual transport routes to the sterilization facilities, this adds to the high cost of a medical product. Again, standard sterilization methods are also disadvantageous from the point of view of material selection and design aspects. The desired sterilization method might damage the material. Gamma-sterilization, for example, can lead to chain breaks or post-curing of the molecular structure of polymers, among other things [4]. And ETO gas sterilization imposes geometric limitations, e.g. due to the kinetics of the sterilization process. As it is not possible to disperse the gas uniformly over the surface, there is no guarantee that the ETO method adequately sterilizes medical devices which have areas that are hard to access.

In view of these drawbacks, the establishment of auto-sterile production would benefit the manufacture of plastic medical products. The basic premise is that the conditions under which injection molding is performed or which obtain upon exit from an extruder die are such that the polymer melt can be considered sterile. If this were combined with a sterile production and packaging environment, auto-sterile production would be possible. Such production methods and packaging are already found in the pharmaceutical sector [1].

Monitoring Contamination

Validation of thermal sterilization processes employing moist heat is based on worst-case contamination of the polymer to be processed. DIN EN ISO 11138-3 specifies the use of bioindicator Geobacillus stearothermophilus (G.s.) (type ATCC 7953) in spore form. This heat-resistant bacterium forms in extreme environmental conditions, such as nutrient deficiency in the late exponential growth phase →

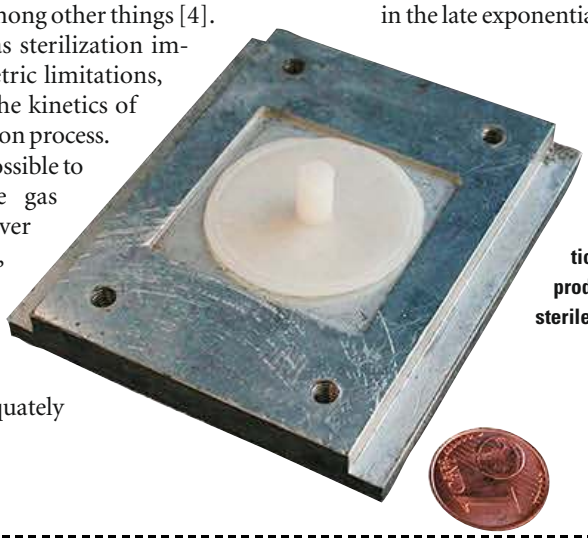

Fig. 1. Sterile production is based on the assumption that the processing conditions are sufficient to produce a part that is sterile upon exiting the die

Translated from Kunststoffe 12/2012, pp. 75–77
Article as PDF-File at www.kunststoffe-international.com; Document Number: PE111225

[2]. This validation approach was chosen for the project because methods for validating sterile polymer melts have yet to be defined or standardized. It can be assumed that the sterilizing effect exerted by the process varies with the chosen process parameters (e.g. temperature, residence times).

For the research project, the pellets were contaminated with G.s. spores during the injection molding process. The trial consisted in imparting a specific level of contamination to the pellets, followed by injection molding under defined conditions and a final microbiological assessment. The injection molding machine (type: Microsystems 50, manufacturer: Wittmann Battenfeld, Kottingbrunn, Austria) was a micro-injection machine with a low maximum shot volume (about 1 cm^3), and separate screw plasticization and piston injection. In addition, the machine had an extended nozzle, which reached into the mold parting line.

Cross-contamination after the injection molding process was avoided by using sterile mold cavities. Autoclavable mold inserts were used for the trial **(Fig. 2)**, which was conducted at a temperature of 200 °C and a mold temperature of 25 °C. The back pressure was 50 bar, the injection speed 300 mm/s and the dwell time 3 minutes. Aluminum was chosen for the insert material because it can be sterilized in steam. A sterile insert was used for each shot into the cavity. The mold parting line was at the same level as the extended nozzle, but did not pass through the mold cavity. The cavity was located entirely inside the mold insert, which consisted of two threaded halves. The runner into the cavity was sealed by a blanking plug until just before melt injection. The purpose of the closed cavity was to avoid contamination of the molded part as the mold was being closed or opened. After the production shot, the entire insert, including molded part, was removed from the mold. The molded part itself was removed from the insert under controlled conditions in the clean bench of the microbiology laboratory **(Figs. 1 and 3)**. Cross-contamination and irregular variations in dwell times between individual shots were avoided by purging with uncontaminated polymer pellets before each production shot. The cavity volume was 1.4 cm^3 and thus exceeded the 1.1 cm^3 maximum shot volume of the injection molding machine. The goal was to minimize shear forces and pressure on the polymer melt in the cavity, as well as make the most of the maximum shot volume. Underfilling also made it easier to remove the molded part from the insert.

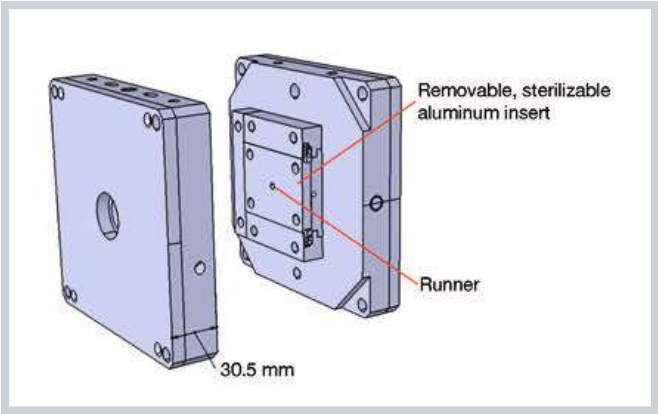

Fig. 2. This injection mold with sterilizable inserts can be used to study decontamination effected by processing. The sterilizable aluminum inserts are used for one production shot each

The trial was conducted on a polyacetal (POM; type: MT24U01, manufacturer: Ticona GmbH, Sulzbach, Germany). This can be autoclaved at 121 °C in a steam sterilizer, thus ruling out the possibility of microbiological contamination prior to specific contamination with G.s. The POM pellets were mixed with 0.5 ml spore suspension, of which effectively about 6,700 spores per gram of pellets adhered to the plastic surface (average spore concentration per gram of pellets: 6,726). For every production shot, 5 grams of pellets were contaminated to ensure the chosen dwell time of 3 minutes was obtained. The degree of contamination of the molded part was determined under the clean bench. An agar culture media was used to count the colony-forming units (CFUs) after 1, 5 and 20 days, this count allowing the number of starting spores to be determined.

No Guaranteed Sterility

Twenty-five molded parts (each weighing 1.6 g) were examined, and one viable G.s. spore was detected on the plastic surface. The total number of G.s. spores before processing was calculated to be 263,424, while only one viable G.s. spore from these was detected after processing. Consequently, the theoretical survival probability fails to meet the target sterility assurance level (SAL), which is an index of the probability that product is still contaminated [4]. The causes may be the heat flow and its duration, shear and compression loads, as well as outer layer formation during injection. Viable G.s. spores may have been trapped below the surface of the plastic. That said, the imparted level of pellet contamination does not reflect the usual level of microbiological contamination of polymer pellets: preliminary trials showed that such pellets only had marginal microbiological contamination on delivery. Therefore, when the injection molding process is considered in tandem with a defined, i.e. contami-

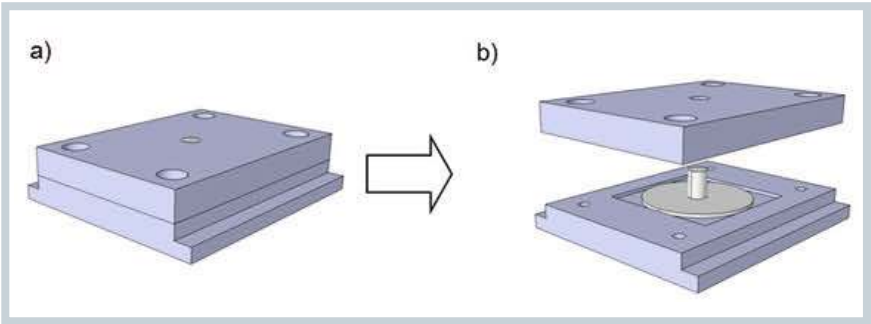

Fig. 3. Schematic representation of removal of the molded part from the cavity in the clean bench: a) closed cavity after removal from the injection molding machine, b) opening of the cavity in the clean bench in order to avoid cross-contamination

nant-reduced, material input under the chosen processing parameters, it can be said that auto-sterilized production of a molded part had occurred. For more precise insights, however, further trials would need to be performed and should involve larger lot sizes, longer dwell times and higher processing temperatures. ■

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