Calculation of the expected shelf life in sterile supply by web-based analysis of long-term exposure data

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Abstract

Sterile barrier systems for terminally sterilized medical products must allow access of sterilants (steam, ethylene oxide). They usually have air-permeable components. Airborne bacteria must be removed to maintain sterility up to the point of use.

A data-based method to continuously control the inflow of environmental air into the packaging was developed to estimate the anticipated shelf life by considering the airborne microbial challenge and the barrier performance of the packaging material. An automated long-term measurement system was developed to calculate the airflow into the packaging caused by temperature fluctuations and weather-dependent air pressure changes according to the Gay-Lussac's law and the Boyle-Mariotte's law. Acceptable shelf lives of sterile barrier systems were calculated based on inputs of the packaging volume, the airborne microbial concentration in the storage area and the filtration efficiency of the packaging material. The web-based calculation of maintenance of sterility resulted in periods between several weeks and months for commonly used packaging when 10 colony-forming units (CFU)/m^3 were entered as the airborne microbial concentration.

The automated long-term measurement system can control the airborne microbial challenge of the stored sterile products and the maintenance of sterility. The web-based shelf life calculation improves the prevention and control of hospital-acquired infections and ensures the supply of safety sterile products which meet the current standards.

Zusammenfassung

Berechnung der erwarteten Haltbarkeitsdauer von Sterilgut durch webbasierte Analyse von Langzeitexpositionsdaten

Sterilgutverpackungen in der Endverpackung sterilisierter medizinischer Produkte müssen für die Sterilisiermittel (Heißdampf, Ethylenoxid) durchlässig sein. Sie bestehen aus luftdurchlässigen Komponenten und müssen luftgetragene Mikroorganismen zur Aufrechterhaltung der Sterilität bis zum Gebrauch der Produkte zurückhalten.

Es wurde ein datengestütztes Verfahren zur fortlaufenden Überwachung des Einstroms von Umgebungsluft in die Verpackung entwickelt, um die Befristung der Lagerungsdauer unter Berücksichtigung der Luftkeimzahl und der Barrierewirksamkeit der Verpackung abzuschätzen. Der durch Temperaturschwankungen und durch wetterabhängige Luftdruckänderungen verursachte Einstrom von Umgebungsluft gemäß dem Gay-Lussac'schen und dem Boyle-Mariotte'schen Gesetz wurde durch ein automatisiertes Langzeitmonitoring erfasst. Nach Eingabe des Verpackungsvolumens, der Konzentration luftgetragener Keime und der Filtrationsleistung des Verpackungsmaterials wurde die akzeptable Lagerungsdauer der Sterilgutverpackungen ermittelt. Für die webgestützte Abschätzung der Aufrechterhaltung der Sterilität durch übliche Sterilgutverpackungen wurden Perioden von einigen Wochen oder Monaten ermittelt, wenn als Eingabe für die Luftkeimzahl ein Wert von 10 KBE/m^3 (koloniebildenden Einheiten, KBE) verwendet wurde.

Durch das automatisierte Langzeitmonitoring kann die mikrobiologische Beanspruchung gelagerter Sterilprodukte und die Aufrechterhaltung der Sterilität überwacht werden. Die webgestützte Berechnung der Lagerungsdauer ist ein wichtiger Beitrag zur Prävention und Überwachung nosokomialer Infektionen und verbessert die Zuverlässigkeit der Sterilgutversorgung entsprechend den aktuellen Standards.

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1. Introduction

Sterilization processes and storage conditions for terminally sterilized products must be validated according to the sterility assurance level (SAL) of 1:1 000 000 (10^{-6}), i.e., the probability for a non-sterile product is equal to or less than 1:1 000 000 [1, 2]. The key role of sterile barrier systems is to maintain the sterility during shipping and storage. The packaging is commonly porous or has porous components in order to allow access of gaseous sterilants such as saturated steam or ethylene oxide to the product [3]. A consequence of this gas permeability is that there is no protection against airflow into the packages.

The volume of the gas mass within porous sterile packages varies dependently on temperature changes and air pressure changes. An increase of air pressure and a decrease in temperature reduce the gas volume, and vice versa. Airflows through the porous part of the packaging are the result when the packaging size is constant. In terms of physics, the volume flow of air into the packaging accords with the Boyle-Mariotte's law "p x V = constant" when weather-dependent air pressure changes are given. According to the Gay-Lussac's law, the temperature-dependent volume change is determined for the isobaric states using the thermal volume-expansion coefficient. Therefore, packaging made of porous packaging material or having gas permeable filter can only maintain sterility if its filtration efficiency and barrier performance are sufficient and not overburdened by the airborne microbial challenge.

The objective of this study was to develop a specific method of quality assurance and risk management of terminally sterilized products during the period of storage and shipping. A data-based and web-based analysis of continuous recording of temperature and atmospheric air pressure changes and the calculation of airborne microbial challenge of the stored sterile items have been developed. The proposed method can help to calculate the expected shelf life and to evaluate the suitability of sterile barrier systems for given shipping and storage conditions.

2. Material and Methods

A real-time data logger (PCE-THB 40, PCE Americas Inc.) was used to record the atmospheric air pressure values and the temperature variations on site in the storage area. The data logger saved the data on the SD memory card. The sampling time was saved only when the measuring value changed more than ±1 hPa. Data processing was carried out using a web-based system. The relevant software was developed and provided in the submenu "input mask" for the desktop monitoring application [4]. The following inputs were entered in the dialogue box: the packaging volume, the filtration efficiency of the porous component which was taken from reference sources, and the airborne microbial concentration in the storage area as colony-forming units (CFU, particle size ≤10 µm) per m^3. After uploading the file for desktop application, the program plotted the measured values of air pressure and temperature and calculated the cumulative airflow into the packaging according to Boyle-Mariotte's law and Gay-Lussac's law on a graph. The airborne microbial challenge (N_0) of the terminally sterilized product was calculated on the basis on the airborne microbial concentration and the cumulative volume of air that entered the sterile packaging during the period of storage. The compatibility of the filtration efficiency of the packaging with the airborne microbial challenge to maintain sterility was calculated according to the following formula:

$$N_0 \times (100 - \text{filtration efficiency in \%}) : 100 \leq 10^{-6}$$ [5, 6]

The anticipated maximum shelf life was shown as an expected date based on the linear regression analysis of the cumulative airflow into the package and the entered airborne microbial concentration (trend line according to the method of least squares).

The atmospheric air pressure values and temperature values between Dec 21, 2021, and Jan 24, 2022 were recorded by the data logger. After ending the air pressure monitoring period, the saving data file was uploaded from the SD card to the input mask of the website. The web-based calculation of the shelf life was performed for double-wrapped paper/film pouches with a volume of 100 cm^3, and double-wrapped baskets with cellulose-based medical-grade paper with a volume of 600 cm^3. The following values of the filtration efficiencies were adopted from the reference: 99.97 % (double-wrapped paper/film pouches), and 99.966 % (baskets double wrapped with medical paper [6]. To calculate the expected shelf lives, an airborne microbiological concentration of 10 CFU/m^3 was given as an example for exposure condition in the storage area for sterile packs.

3. Results

Figure 1 and Fig. 2 show the graphs of the viewing screen of the web-based analysis. Figure 1 shows the temperature and air pressure time courses measured by the data logger between Dec 21, 2021, and Jan 24, 2022. Figure 2 shows the calculated cumu-

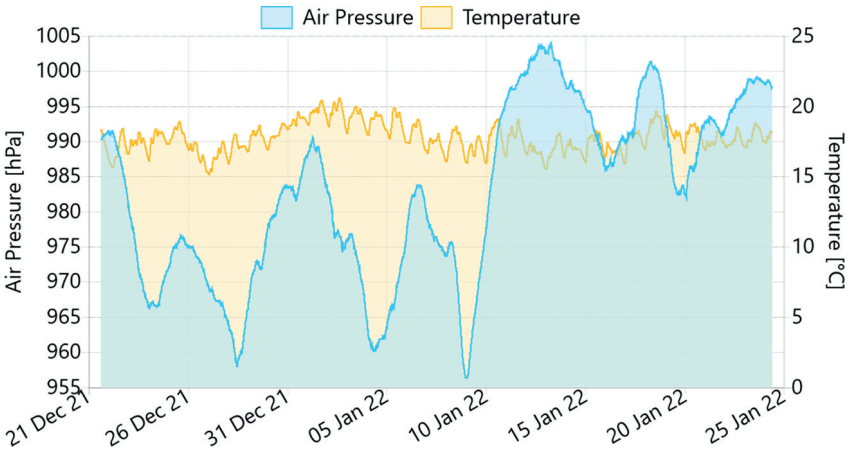

Figure 1: Web-based monitoring of temperature and weather-dependent air pressure changes recorded between Dec 21, 2021 and Jan 24, 2022 (source of all figures: the author).

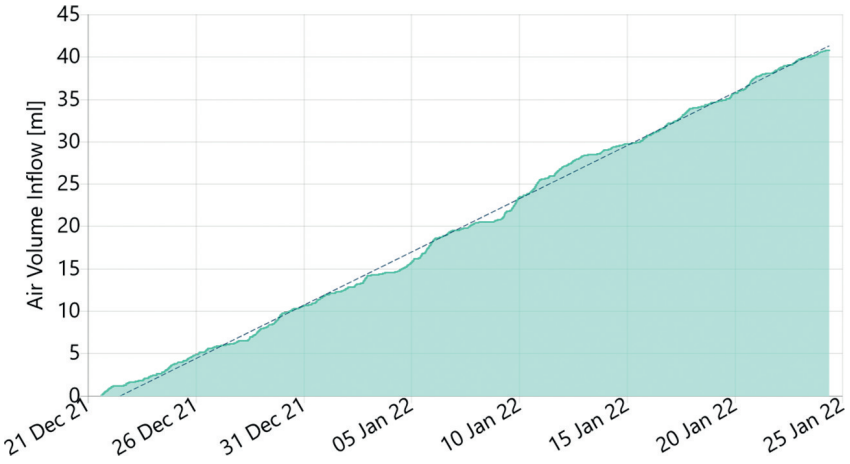

Figure 2: Calculated cumulative inflow of air volume (ml) into the double-wrapped pouch of 100 cm³.

lative airflow into the packaging with a volume of 100 cm³ after the beginning of the recording. Following volumes that entered into the packaging in the monitored period of 34 days were calculated by the program: 40.8 cm³ of air for the 100 cm³ pouches and a volume of 247.8 cm³ for the double-wrapped baskets of 600 cm³. The program calculated Sept 14, 2022 as expiration date for the double-wrapped paper/film pouches when an airborne microbiological concentration of 10 CFU/cm³ was given. The expiration date for the double wrapped baskets was Jan 30, 2022.

4. Discussion

The maintenance of sterility during the post-sterilization period is as crucial as the sterilization itself. A successful sterilization will fail if thereafter recontamination of the sterilized product takes place. The WHO stated that the health care environment plays a significant role in the transmission of microorganisms and that the proper storage of sterile items is essential to guarantee the maintenance of sterility [7]. Current shelf life policies which address the storage conditions of terminally sterilized products recommend a clean and dry environment, a moderate temperature without wide fluctuations and an event-related outdating [8, 9]. The International Standard ISO 11607-1:2019(E) states that the loss of sterility is regarded as event-related rather than time-related [2]. The concept of event-related sterility policy means that sterility is maintained unless specific events occur and compromise the sterility: *"Time does not affect sterility, but an event such as handling or incorrect storage conditions may"* [8]. Typical events are punctures, tears, cuts or breaks on gaskets and broken seals.

Routine bacteriological monitoring of the air quality is not recommended as standard operating procedure to control the storage conditions in the sterile services department [2, 9]. Certain factors operate more in a time-related way such as exposure to airborne contaminants, temperature changes and weather-dependent air pressure changes [3]. Therefore, Boyle-Mariotte's law and Gay-Lussac's law, i.e., air pressure changes and temperature fluctuations have been integrated in the web-based calculation of the airborne microbial challenge of the stored sterile products.

It was shown that the shelf life can be extended by means of reduction of the airborne microbial concentration in the storage area [6]. The online-available method enables the health care professional to establish a data-based quality control system for the calculation of shelf lives of sterilized items.

5. Conclusions

A data-based monitoring of weather-dependent air pressure changes and temperature fluctuations allows to calculate the airborne microbial challenge of wrapped sterile products and to assess whether

the filtration efficiency of the selected sterile barrier systems is compatible with the maintenance of sterility during the storage period. A web-based calculation of expected shelf life is recommended for the monitoring of the shipping and storage conditions in order to maintain sterility and to prevent hospital acquired infections.

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