

CRITERIA FOR EVALUATION OF NEW STERILIZATION TECHNOLOGIES

Cr terios para avalia o de novas tecnologias para esteriliza o
Criterios para evaluaci n de nuevas tecnolog as para esterilizaci n

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ABSTRACT: Objective: To discuss criteria and methods that should ideally guide the evaluation of new sterilizing technologies. **Method:** Narrative review by means of search and interpretation of national legislation related to sterilization processes, as well as technical standards and documents that support constructive, functional, and safety aspects of sterilization technologies. **Results:** Topics relevant to the safety of sterilization processes, such as sterility testing, simulation of cycle under the worst load conditions, compatibility with sterile barrier systems, biocompatibility tests, process control, and economic evaluation, were discussed. **Conclusion:** The results will directly benefit three major segments: manufacturers while developing and requesting registration of new technologies; The National Sanitary Surveillance Agency when officially adopting a list of requirements with the manufacturer at the time of new equipment registration request; And health services, which will consume these new sterilization technologies.

Keywords: Sterilization. Methods. Technology. Science and technology legislation. Equipment technology and provision.

RESUMO: Objetivo: Discorrer sobre cr terios e m todos que devem nortear a avalia o de novas tecnologias para esteriliza o. **M todo:** Estudo de revis o narrativa mediado pela busca e interpreta o da legisla o nacional relacionada aos processos de esteriliza o, normas t cnicas e documentos que embasam os aspectos construtivos, funcionais e da seguran a das tecnologias para esteriliza o. **Resultados:** Foram discutidos t picos relevantes   seguran a dos processos de esteriliza o, como a prova de esterilidade, simula o do ciclo nas piores condi es de carga, compatibilidade com sistemas de barreira est ril, testes de biocompatibilidade, controle de processos e avalia o econ mica. **Conclus o:** Os resultados beneficiar o diretamente tr s segmentos principais; os fabricantes, no desenvolvimento e na solicita o de registro de novas tecnologias para esteriliza o; a Ag ncia Nacional de Vigil ncia Sanit ria, na ado o oficial de uma lista de exig ncias junto ao fabricante no momento de peti o de registro de novos equipamentos; e os servi os de sa de, no consumo de novas tecnologias para esteriliza o. **Palavras-chave:** Esteriliza o. M todos. Tecnologia. Legisla o em ci ncia e tecnologia. Tecnologia de equipamentos e provis es.

RESUMEN: Objetivo: Discurrir sobre criterios y m todos que deben guiar la evaluaci n de nuevas tecnolog as para esterilizaci n. **M todo:** Estudio de revisi n narrativa mediado por la b squeda e interpretaci n de la legislaci n nacional relacionada a los procesos de esterilizaci n, normas t cnicas y documentos que basan los aspectos constructivos, funcionales y de la seguridad de las tecnolog as para esterilizaci n. **Resultados:** Fueron discutidos t picos relevantes a la seguridad de los procesos de esterilizaci n, como la prueba de esterilidad, simulaci n del ciclo en las peores condiciones de carga, compatibilidad con sistemas de barrera est ril, pruebas de bio-compatibilidad, control de procesos y evaluaci n econ mica. **Conclusi n:** Los resultados beneficiar n directamente tres segmentos principales; los fabricantes, en el desarrollo y en la solicitud de registro de nuevas tecnolog as para esterilizaci n; la Agencia Nacional de Vigilancia Sanitaria, en la adopci n oficial de una lista de exigencias junto al fabricante al momento de peti n de registro de nuevos equipos; y los servicios de salud, en el consumo de nuevas tecnolog as para esterilizaci n.

Palabras clave: Esterilizaci n. M todos. Tecnolog a. Legislaci n en ciencia y tecnolog a. Tecnolog a de equipos y provisiones.

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Received: 15 June 2017 – Approved: 11 July 2017

DOI: 10.5327/Z1414-4425201700030009

INTRODUCTION

The challenging mission of the Sterile Processing Department (SPD) is to turn critical, used products into clean, sterilized products with preserved function. It therefore needs sterilization equipment that is absolutely safe as to elimination of microorganisms and which can preferably be installed in the health service aiming at practicality and total process control.

In addition, it is desirable that cycles be fast enough to meet the high demand and dynamics of care units, especially the surgical center; have no limitations on penetrability of the agent in medical devices; be compatible with sterile barrier systems available in the market; have low toxicity, be monitorable by biological and chemical indicators — especially type 5 or 6; and have affordable acquisition, installation, operation processes, besides the possibility of periodic qualification. These characteristics should guide the assessment of new sterilizing technologies in the field of health either by the Brazilian Health Surveillance Agency (ANVISA) at the time of its registration for marketing purposes, or by the SPD responsible technician in order to support its acquisition.

Analyzing product offer throughout evolution, especially surgical techniques, the significant increase of health products with thermosensitive characteristics is notable, leading to a need of new technologies for low temperature sterilization. The saturated steam autoclave currently meets demands of heat-resistant products at the SPD, with continuous improvements such as the coupling of fractional vacuums, leaking tests, and devices that remove non-condensable gases from the steam before entering the inner chamber. The same cannot be claimed for healthcare thermosensitive products, once the equipment must operate at low temperatures with a chemical agent.

The first equipment to sterilize thermosensitive medical devices in nationwide health services was ethylene oxide, followed by hydrogen peroxide gas plasma, low-temperature steam and formaldehyde. Although these technologies are regulated by the Ministry of Health through ANVISA in Brazil, each of them poses limitations, which impels the industry to invest in new technologies.

Although ethylene oxide's penetration is considered the gold standard, according to requirements of the Joint Interministerial Ordinance of Ministry of Labor and Employment (MTE) and Ministry of Health (MS)

nº 482, 1999, it is currently to the charge of outsourced companies that fully meet legal requirements¹. Although the other two technologies may be allocated at the SPD, they require caution due to the limitations they impose, features related to dissemination and compatibility with raw materials of medical devices and barrier systems.

New health technologies should be evaluated for efficacy, comparative effectiveness, and economic aspects in compliance with methodological guidelines proposed by the Brazilian Network for Health Technology Assessment (REBRATS), which is linked to the Ministry of Health²⁻⁴. However, such methodologies have general application and do not apply only and specifically to sterilization equipment.

So far, there is not a clear definition of criteria and methods to be officially adopted by ANVISA for the evaluation of new equipment for sterilization. In view of the above, we question what these would be. Thus, our study proposes to discuss sound criteria and methods that should guide the evaluation of different aspects before the approval and use of new technologies for sterilization in health services.

METHOD

Narrative review based on search and interpretation of the national legislation related to sterilization processes, national and international technical standards and documents that support constructive, functional and safety aspects of sterilization technologies. The aim was to establish the tests and minimum criteria for a new sterilization technology to be considered safe for use in health services.

Sterilization tests

Considering that bacterial spores are recognized as the most resistant and feasible microbial form for handling in non-specialized laboratories, they should be part of the process in a sterilization test. Viruses, oocysts of the subclass *Coccidia*⁵ or prions are certainly greater specific challenges than bacterial spores, but the risk posed (in the case of prions), the absence of officially standardized methods (in the case of *Coccidia*) and non-availability of specialized laboratory infrastructure for virus testing (although there is an official European methodology) cause these to not

be officially included in most countries in the process of approval of new technologies with purposes of sterilization in health services.

In Brazil, the sterility test report to be presented by the manufacturer of a new technology must follow the standards established by the National Institute for Quality Control in Health (INCQS), Fundação Oswaldo Cruz (FIOCRUZ), which integrally complies with the Association of Official Analytical Chemists International (AOAC)⁶, official methodology of the Food and Drug Administration (FDA).

The traditional AOAC⁶ methodology addresses two bacterial spores to be tested: *Bacillus subtilis*, American Type Culture Collection (ATCC) 19,659 and *Clostridium sporogenes*, ATCC 3,584. Tests should be performed with two types of carriers: 120 porcelain carriers purchased from Fischer Scientific CoTM, No. 7,907, and another 120 carriers made with approximately 6.5 cm of surgical silk thread n° 2 for each test microorganism. All cultures and their subcultures (total of 240 cultures for each test microorganism) should be put in initial 21-day incubation, followed by heat shock at 80°C and complementary 72-hour incubation. After these procedures, if there is not recovery of 100% of test samples, the technology for sterilization under evaluation is considered effective. The challenge of spored microorganisms carried by penicylinders and surgical silk thread n° 2 should be validated against the hydrochloric acid HCl at 2.5N concentration, subjected to contact with acid for 2, 5, 10 and 20 minutes. For inoculum reliability, the spores must stand for at least two minutes and can withstand for more than 20 minutes.

As a result of an outbreak of rapidly growing bacteria (RGB) infections related to invasive procedures in health services across almost all Brazilian States, with peak in 2006, ANVISA's General Management of Sanitation (GGSAN), determined the inclusion of *Mycobacterium massiliense*, strain INCQS 00594,⁷ as a test microorganism in the evaluation of sterilization products through Resolution of the Collegiate Board of Directors (RDC) n° 35, 2010⁷. INCQS has not yet expressed its opinion on this inclusion in the group of test microorganisms to assess new sterilization technologies. However, reports must attest to minimal sterilizing effectiveness against spores of *Bacillus subtilis*, *Clostridium sporogenes*, and now also *Mycobacterium massiliense*.

Tests on devices simulating the penetration of sterilizing agent under the worst load conditions

To evaluate the penetration of the sterilizing agent in products, standardized devices and tests should be used. Considering the direct contact between sterilizing agent and surface required by low-temperature methods, the test device should reproduce the challenging conditions related to air removal and sterilizing agent penetration, whether by length, lumens, blind bottom, recess, or articulation.

For saturated steam, tests on devices that simulate steam penetration in the worst loading conditions are already well established. The same cannot be claimed for low-temperature equipment, though.

One of the tests proposed to verify air withdrawal and penetration of the sterilizing agent at low temperature consists in sterilization of an approximately 90-cm long tube with a 0.65-cm internal diameter and sealed end, where a biological indicator containing the spore that is most resistant to the sterilizing agent and a chemical indicator (preferably type 5 or 6, specific to sterilization method) are placed⁸.

The American National Standards Institute / Association for the Advancement of Medical Instrumentation (ANSI / AAMI) Standard ST41:2008⁹ establishes a test to monitor sterilization equipment in which biological indicators are placed inside a plunger syringe. These syringes are placed on a tray and packaged with a sterile barrier system, thus forming the challenge package.

In addition to lumens with and without a blind bottom and other internal spaces, sterilizing superimposed surfaces such as surgical instruments' articulations, grooves, and racks is also a major challenge in low-temperature processes. Thus, it is reinforced that devices used in the validation of any sterilization process must be able to support challenging conditions in comparison to medical devices used in healthcare assistance. In other words, a technology intended for the sterilization of endoscopes, for example, must challenge the complex conformation of this device and be proven safe for daily life.

Tests of compatibility with sterile barrier systems

A critical aspect that must be evaluated in processes of new sterilization technologies approval is related to the

sterile barrier system, that is, the physical and structural behavior of materials used for medical devices packaging.

The sterile barrier system ensures sterilization until the moment of use and promotes the transfer of contents by an aseptic technique¹⁰. Therefore, validation of packaging process is also crucial to ensure the integrity of the sterile barrier system until it is used¹¹.

The current context of sterile barrier systems involves a diversity of color options, dimensions, weights, hermeticity, and biobarrier property/effectiveness characteristics. It is recommended that the manufacturer of new sterilization technologies perform functional, macroscopic analyses, as well as maintenance of bio-barrier and sterilant residues remaining in the package so that the initially validated properties are rigorously maintained.

Events such as discoloration, physical changes, loss of peculiar resistance, deterioration of the seal, and mischaracterization of product identification after the cycle are important indicators of non-compatibility with the sterilization method.

Biocompatibility tests

Safety in sterilization processes depends not only on the guarantee of sterility but also on the absence of toxic effects whenever the medical device comes in contact with the patient during invasive procedures, since sporadic activity presupposes toxicity of the sterilizing agent. In addition to sterilization employing chemical or physical agents to destroy microbial cells, the device must be free of chemical residues that compromise its use at the end of the process, just as the raw material must maintain its initial biocompatibility. The same is valid for sterile barrier systems, since they must be permeable by the sterilizing agent.

To meet this demand, specific tests are carried out to quantify residues and to evaluate the biological response induced by medical devices, according to their nature and time of contact with the tissues¹².

Considering the nature of the device in contact with tissues (superficial contact by external or implantable communication) and the time of contact, which is sorted as limited (<24 hours), prolonged (>24 hours to 30 days), and permanent (>30 days), safety assays may include: cytotoxicity, intracutaneous sensitization, irritation or reactivity, systemic toxicity, subacute and subchronic

toxicity, genotoxicity, hemocompatibility, and implantation. Selection criteria of appropriate tests are described by ISO 10993-1¹².

For sterile barrier systems that do not come into direct contact with tissues, absence of cytotoxicity must be assured as they come into direct contact with medical devices until they are used.

In addition, material safety data sheet (MSDS) must be presented, as well as compliance with provisions of Decree 2.657, from July 3, 1998,¹³ which promulgates International Labor Organization (ILO) convention 170 regarding chemicals safety at work.

Sterilization process control

The ANVISA Resolution of the Collegiate Board of Directors 15¹⁰ requires that the physical parameters of a sterilization cycle be recorded at each cycle. Thus, one of the main requirements for the regularization of new equipment is monitoring all critical variables of the process with a printed data record, indicating — preferably at the end of the cycle —, whether variables' values meet acceptance criteria, also informing if it was satisfactory or not, based on this information. This is a requirement for the physical indicator to be valid and which can be used as a counterproof to a chemical or biological indicator. Another relevant aspect is the possibility of monitoring variables by instruments that are independent of the equipment, since they must be qualified every 12 months, and calibrated as frequently as determined by the manufacturer, in periodic maintenance. In addition, if the installation site changes, goes through intervention that changes critical parameters as of evaluation of changes implemented in qualification, or presents suspected flaws, it should be requalified. Besides such monitoring, chemical and biological indicators should be used at each requalification¹⁰.

The Brazilian legislation¹⁰ also establishes that the control of sterilization processes be carried out upon each load, in a challenge test package with chemical integrators type 5 or 6 — previously characterized as “class” by ISO 11.140-1¹⁴, revised in 2014.

Ideally, new technologies should be marketed only after development and availability of chemical indicators:

- Type 1 (which differentiate products that are or are not exposed to the sterilizing agent without signaling the effectiveness of sterilization);

- Type 2 (specific tests for particular conditions that are essential to the success of a given method);
- Type 3 (which react in the presence of one critical process variable);
- Type 4 (which react in the presence of more than one critical process variable);
- Type 5 (which react to all critical process variables);
- Type 6 (which emulate the sterilization cycle, reacting to all critical process variables at shorter variation intervals)¹⁴.

Specific and/or validated biological indicator should also be required, as it is one of the important pillars in the evaluation and monitoring of sterilization cycles¹². In addition, the most challenging step of a sterilization process must be defined while qualifying the equipment, so that the biological indicator and the load-clear test package are properly positioned during the cycle. As the indicator must be packaged so it promotes challenging process conditions¹⁰, the manufacturer must present its own commercially available challenge package or compliance with packaging guidelines by SPD itself at the time of registration request.

Economic evaluation of sterilization technologies

Economic aspects are fundamental in the decision-making process to incorporate a new technology. Despite this, the literature still lacks both national and international publications addressing cost-related evaluations of equipment, products, and sterilization processes. The few publications available speak to costs of reuse of single-use medical devices, where manufacturers do not recommend this process compared to disposal, and also studies that evaluate costing systems applied to CME^{15,16}. Worthy of note is Canadian Technology Assessment, which has calculated the costs of pasteurizers compared to washer-disinfector machines to reprocess respiratory care devices. Results of operational costs/year were very similar: C\$ 10,657 for washer-disinfector machines versus C\$ 9,425 for pasteurizers. The study highlights the different applications of washer-disinfector machines as a differential benefit in parallel to pasteurizers¹⁷.

Studies addressing cost-effectiveness should be more explored by professionals involved with medical devices, since high cost is a constant challenge for health care services. Results of such analyses provide important managerial tools, enabling a

technical basis for negotiations, technological management at SPD, and optimization of financial resources¹⁸.

There are several methodologies available for economics-related studies with health technologies, and they may be based either on the principles of health economics or cost accounting. Comparative economic evaluations are preferred, that is, studies that analyze costs and results of new technologies as opposed to those already available in the national or international market for the same purposes^{3,18,19}.

The correct identification of cost components in a process is a fundamental step for all methodologies. In the case of sterilization technologies, they should at least include the value of equipment and accessories acquisition, use and cost of all necessary inputs, expenses with environmental adjustments for installation, personnel dedicated to operating the equipment, value destined to team training, environmental impact, maintenance and monitoring costs^{3-4,16,18}.

Data for economic evaluation is retrieved from detailed sources that are compatible with the context of technology application, thus avoiding inference and fictional data. Therefore, when deciding whether to incorporate a technology in a particular health service, knowing the institutional demand, the operational capacity of each equipment model, and the forecast of cycles/day is fundamental.

Caution must be taken when interpreting data from health technologies economic studies; avoiding generalization of results from assessments carried out in different contexts is important, as there may be important variations related to work processes and local costs. It is recommended that studies with this scope be also evaluated for quality through an instrument developed for such purpose²⁰.

Very optimistic statements also require cautiousness, for example, upon incorporating a certain technology, promise of arsenal minimization, team reduction, cancellation of contract with outsourced companies, minimum time of product return for use, and others. Cost-related evaluations allow us to anticipate future reality; but not accurately, in view of possible uncertainty of parameters and analytical models adopted³.

CONCLUSION

Having patient safety as the guiding principle of health care, be it direct or indirect, this study discussed criteria

and methods for the evaluation of new equipment for sterilization in the health field that will directly benefit three main segments:

1. The manufacturers, when developing and requesting registration of new sterilization technologies with ANVISA;
2. ANVISA, with the official adoption of a list of requirements for manufacturers at the time of request of registration of new sterilization equipment aimed for health services; and
3. SPD, when consuming the new technologies for sterilization in health care.

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