LOW TEMPERATURE STEAM AND FORMALDEHYDE (LTSF) STERILIZER
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DISCLOSURE

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EXECUTIVE SUMMARY

Introduction

Medical instruments and product must be sterilized using methods compatible with the construction materials. If such items are heat-resistant, autoclaving is preferable. However, many such items are heat-labile, being constructed of polyethylene, polyester or polyamide. For these, Matachana Low Temperature Steam and Formaldehyde Model 130 LF Sterilizer has been developed for the sterilization of heat-sensitive product that cannot withstand the temperatures required for steam sterilization (121°C), but can be treated at temperatures of 60°C or 78°C and are resistant to vacuum and humidity. This sterilizer works with low temperature steam and using 2% formaldehyde. This procedure achieves terminal sterilization of the products. The items to be sterilized are packed using traditional wrapping systems, and cycle monitoring is performed using standard chemical and biological indicators (Bacillus stearothermophilus). It is claimed that the Matachana 130 LF is the first sterilizer built in accordance with the International Technical Specifications of the European Norm for LTSF sterilizers, EN 14180: “Sterilizers for medical purpose - Low Temperature Steam and Formaldehyde sterilizers – Requirements and testing”.

Objective / Aim

The objective of this technology review was to assess the safety, efficacy and cost-effectiveness of Low Temperature Steam and Formaldehyde Sterilizer – Matachana 130 LF.

Results and Conclusions

There was limited retrievable evidence to show that Matachana Low Temperature Steam and Formaldehyde Model 130 LF Sterilizer and other brands of low temperature steam with formaldehyde sterilizers are safe. The search strategies yielded one article on the CE Safety Data Sheet issued to Matachana Model 130 LF Sterilizer.

There was poor to fair level of retrievable evidence on the efficacy of Matachana Low Temperature Steam and Formaldehyde Model 130 LF Sterilizer and other brands of low temperature steam with formaldehyde sterilizer.

However, there was no retrievable evidence on the cost-effectiveness of Matachana Low Temperature Steam and Formaldehyde Model 130 LF Sterilizer and other brands of low temperature steam with formaldehyde sterilizer.
**Recommendation**

Based on the review, Matachan Low Temperature Steam and Formaldehyde Model LF 130 Sterilizer may be considered to be used in Ministry of Health hospitals for research purpose, taking into account the capacity of the sterilizer with certain provisos:-

i) Whatever the process, it must result in an approved sterile product, free from hazardous levels of residues.

ii) It must be reasonably easy to use and capable of physical monitoring; at the same time have a short process time. It should be possible for the normal packaging staff to operate and control.

iii) The process should allow the product to be packaged in normal wrapping material so as not to create additional costs.

iv) It must result in a product available for immediate use.

v) It must be safe to use with standard pre-processing and have good safety margins.

However, there is a concern on the use of LTSF sterilizer which should be assessed and certified by our local environmental safety agency. This technology also needs to be certified by the necessary agency on the safety aspects, with regards to its formaldehyde concentrations, and trained authorized person who should be also certified to handle this kind of equipment. More clinical research and studies should be carried out at our various local clinical settings and validate the equipment performance since evidence showed that its efficacy can vary with different microbiological load.

**Methods**

Electronic databases were searched, which included PubMed, Medline, Journal @ Ovid full text via OVID, OVID EBM Reviews - Cochrane central register of controlled trials, EBM Reviews - Cochrane database of systematic review, Horizon scanning databases - Centre, Birmingham, Australia and New Zealand Horizon scanning (ANZHSN), FDA website, MHRA website and from non scientific database - Google search engine. In addition, a cross-referencing of the articles retrieved was also carried out accordingly to the topic. Relevant articles were critically appraised and evidence graded using US / Canadian Preventive Services Task Force.
LOW TEMPERATURE STEAM AND FORMALDEHYDE (LTSF) STERILIZER

1.0 INTRODUCTION

Many clinical instruments and devices contain, or are made of, heat-labile materials that cannot be sterilized by autoclaving. Low temperature steam and formaldehyde (LTSF) sterilization is one of the available alternatives most used in many European countries, although, due to the danger posed by formaldehyde, there were some doubts at first as to the applicability of using this system. In 2004 the United States Environmental Protection Agency (USEPA) and the International Agency for Research on Cancer (IARC) have declared formaldehyde as a carcinogen. In addition, it is known to have some detrimental side effects, including respiratory dysfunction, contact dermatitis and possible allergic reactions.¹

Nonetheless, the most modern employed LTSF sterilization systems use solutions containing formaldehyde at low concentrations (2%), which are supplied in disposable bags that do not require manipulation by the personnel in charge of sterilizing materials as they are automatically dosed. Moreover, the requirements and testing of these sterilizers for medical purpose were published in 2003 by the European Committee for Standardization on the European Standard EN 14180.²

Matachana Low Temperature Steam and Formaldehyde Model 130 LF Sterilizer has been developed for the sterilization of heat-sensitive product that cannot withstand the temperatures required for steam sterilization (121°C), but can be treated at temperatures of 60°C or 78°C and are resistant to vacuum and humidity. This sterilizer works with low temperature steam and using 2% formaldehyde. This procedure achieves terminal sterilization of the products. The items to be sterilized are packed using traditional wrapping systems, and cycle monitoring is performed using standard chemical and biological indicators (Bacillus stearothermophilus). It is claimed that the Matachana 130 LF is the first sterilizer built in accordance with the International Technical Specifications of the European Norm for LTSF sterilizers, EN 14180: “Sterilizers for medical purpose - Low Temperature Steam and Formaldehyde sterilizers – Requirements and testing”.³

This technology review was conducted following a request from the Director of Medical Development Division, Ministry of Health Malaysia, following a proposal by a Matachana company to promote the usage of Low Temperature Steam and Formaldehyde Sterilizer Model 130 LF which is made in Spain to Ministry of Health Hospitals.

2.0 OBJECTIVE /AIM

The objective of this technology review was to assess the safety, efficacy and cost-effectiveness of Low Temperature Steam and Formaldehyde Sterilizer – Matachana 130 LF.
3.0 TECHNICAL FEATURES

LTSF sterilization cycle consists of six phases:-

i)  Pre-vacuum

ii) Pre-pulses of steam

iii) Formaldehyde feed

iv)  Sterilization

v)  Washing pulses

vi) Air pulses.

Air is eliminated from the chamber during the pre-vacuum period, and then sub-atmospheric steam is added repeatedly to the humid hot chamber during the pre-pulsing period. During the formaldehyde feed and sterilization processes, formaldehyde is added and the chamber condition is maintained at a specified temperature for a predetermined duration. During the washing pulses period, saturated steam is injected and exhausted repeatedly in order to remove formaldehyde. Finally formaldehyde residue is removed and the contents are cooled and dried through cycles of air and vacuum.3
The Matachana 130 LF sterilizer has several features such as below:

- The 130 LF works with a sterilization solution containing a minimal formaldehyde concentration (2%) that is supplied in disposable bags.
- The bag is placed in the consumption components compartments and its content is emptied automatically into the corresponding container, without the user’s additional handling.
- The venting performed in the cycle is sufficient to vent the item. No additional aeration time is required.
- Controlled by microcomputer and colour touch screen which allows easy access to the different working menus of the sterilizer.
- Linear graphic recorder with two channels (pressure and temperature).
- The emissions are diluted in a special tank before being disposed of down the drain and the system complies with international regulation for such waste.
- All that is required to install the system is a water supply and a standard drain. The 130 LF need no venting to the exterior and no special location is required. It can be installed in the CSSD near steam sterilizer.
- Process management with PC through and optional dedicated software – CSSDoc.
- Traditional wrapping systems are used
- Cycle monitoring is performed using standard chemical and biological indicators.
- One or two door versions.

Programmes
- Program 60°C
- Program 78°C
- Vacuum test

Dimensions (Width, Height, Depth) mm
- Chamber : 320 x 320 x 900
- Total dimensions : 750 x 1850 x 1100

Weight (kg) : 400
Volume (litres) : 130
Power : 6.6 KW

4.0 METHODOLOGY

4.1 Searching

Electronic databases were searched, which included PubMed, Medline, Journal @ Ovid full text via OVID, OVID EBM Reviews - Cochrane central register of controlled trials, EBM Reviews - Cochrane database of systematic review, Horizon scanning databases - Centre, Birmingham, Australia and New Zealand Horizon scanning (ANZHSN), FDA website, MHRA website and from non scientific database - Google search engine. In addition, a cross-referencing of the articles retrieved was also carried out accordingly to the topic.
The following keywords were used either singly or in combinations: Low Temperature Steam and Formaldehyde Sterilizer, sterilization, disinfection, safety, efficacy and cost-effectiveness.

4.2. Selection

All published articles related to safety, efficacy and cost-effectiveness of Low Temperature Steam and Formaldehyde Sterilizer were included. Relevant articles were critically appraised using Critical Appraisal Skills Programme (CASP) and evidence was graded according to US/Canadian Preventive Services Task Force (Appendix 1).

5.0 RESULTS AND DISCUSSION

The search strategies yielded one article on the CE Safety Data Sheet issued to Matachana Low Temperature Steam and Formaldehyde Model 130 LF Sterilizer. There were two articles related to the safety and four articles related to the efficacy retrieved. However, there was no retrievable evidence on the cost-effectiveness of Low Temperature Steam and Formaldehyde Sterilizer.

5.1 Safety

It is claimed that the Matachana Low Temperature Steam and Formaldehyde Model LF 130 Sterilizer comply with the European Directive on Electromagnetic Compatibility 89/336/EEC and the directive on Safety Machines 89/392/EEC. Sterilizer is considered as Class IIa Medical Device, and for this reason, they need to meet the standards set out in the European Directive of Medical Devices 93/42/EEC, which has been obligatory since 1998. The CE Safety Data Sheet was issued to Matachana Low Temperature Steam and Formaldehyde Model LF 130 Sterilizer according to Directives 91/155/EEC and 2001/58/EC about classification, packaging and labelling of dangerous substances.

A cross-sectional study was conducted by Kanemitsu K. et al. 2005, measured the amount of residual formaldehyde on 16 plastic material and five medical devices following LTSF sterilization. The study revealed that the amount of residual formaldehyde on polyamide 6, polyurethane, natural rubber and polyacetal was higher (21.9, 15.2, 3.0 and 2.1 times, respectively) than that on the filter paper. Besides, residual formaldehyde was retrieved from four medical equipments, but not from the tweezers. The amount of formaldehyde recovered from a breathing circuit, anaesthesia circuit, oxygen tubing, airway tube and tweezers was 260, 240, 594, 56 and 0 µg, respectively (European Standard EN 14180: < 200 µg). This study indicated that the main material composing the medical equipment should be verified when LTSF sterilization is performed, because the amount of formaldehyde residue varies according to the surface area and the material used for construction.

In a cross-sectional study conducted by Mariscal A. et al. 2005, the residual formaldehyde on eight common clinical materials were analysed after sterilization with
LTSF, using two methods; microtiter-based fluorescence bioassay and chemical desorption test. The results showed that formaldehyde residues were detected on cotton, filter paper, natural rubber, polivinyl chloride and silicone-coated latex, but not on polyurethane, silicon or glass. Formaldehyde never exceeded the recommended maximum concentration on clinical devices of about 5 µg/cm². The study found that formaldehyde concentrations detected by both methods on the different test materials were very similar, the differences were in no case statistically significant (p ≤ 0.05). The measurements of formaldehyde residues showed a good correlation between fluorescence bioassay and chemical desorption test results, with a linear fitting curve and an $R^2 = 0.9396$.

5.2. Efficacy

Kanemitsu K. *et al.* 2003 evaluated LTSF sterilizer based on the draft European Standard prEN 14108. He conducted a microbiological and desorption test to validate the sterilization process and determine the residual amount of formaldehyde. The LTSF sterilizer GEF 449 (Getinge AB, Getinge, Sweden) was used and was installed in the Central Supply and Sterilisation Department of Tohoku University Hospital (Sendai, Japan). Five programs (P1 - P5) were set up, for full and small loads, with variations in temperature of sterilization, duration of sterilization, and number of washing pulses. The results indicated that for microbiological test, with small loads all test showed no growth of *Bacillus stearothermophilus* (ATCC7953) spores. However, positive cultures were observed with full load tests using P5 (sterilization temperature, 50°C). In a desorption test, the mean concentrations of formaldehyde in five programs (P1 - P5) were 31.9, 56.3, 54.9, 82.2 and 180.6 µg per filter paper, respectively, which are below the limits allowed by the draft Standard (< 200 µg). This study concluded that although the load influenced the efficacy of the LTSF sterilizer, the LTSF sterilizer is useful for sterilization because of its excellent efficacy, short handling time, and safety.

Another study was conducted in 2005 by Kanemitsu K. *et al.* to validate the LTSF sterilization for endoscopes, using VDES (validation device for endoscope sterilization). Microbiological tests were conducted to validate the sterilization process. Spore of *Geobacillus stearothermophilus* (ATCC7953) was used as the biological indicator. Two prototypes of VDES were used, type A and type B, designed to resemble the gastroscope and duodenoscope, respectively. He hypothesized that, if LTSF can effectively sterilize the endoscope, it must be able to kill all *Geobacillus* spores held deep inside the VDES. The culture results for VDES type A and type B after LTSF sterilization were all negative, while positive cultures were obtained in all control experiments. Culture of the biological indicator confirmed the complete eradication of the bacteria in a total of 10 experiments with each type of VDES after LTSF sterilization. The authors concluded that the LTSF sterilizer can be the first choice for sterilizing endoscopes, based on validation results using the VDES, and it is necessary to perform an endurance test and measure the level of residual formaldehyde after LTSF sterilization.

Kanemitsu K. *et al.* 2005 conducted a controlled study of ethylene oxide gas (EOG), hydrogen peroxide gas plasma (PLASMA), and low-temperature steam formaldehyde (LTSF) sterilization. The efficiencies of EOG, PLASMA and LTSF sterilization were tested using metal and plastics plates (stainless steel, copper and polyethylene), common medical instruments (forceps, dissector and airway tube), and three process challenge
devices with narrow lumens (Helix PCD and two modified Helix PCD with internal diameter of 0.96 mm and hose, 1.5 m and 3.0 m respectively). All items were contaminated with *Bacillus stearothermophilus* (ATCC 7953) spores or used a standard biological indicator. The results showed that sterilization of all plates using EOG and LTSF resulted in complete eradication of *B. stearothermophilus* (ATCC 7953) spores in both the presence and absence of serum. However, two samples subjected to PLASMA sterilization yielded positive cultures. Experiments using medical instruments demonstrated similar results with EOG and LTSF, with negative cultures on forceps, dissectors, and airway tubes in all cases. The PLASMA system did not adequately sterilize the forceps and dissector in one of three trials. Similarly, experiments with process challenge devices demonstrated that EOG and LTSF completely eradicated the spores from the Helix PCD and two modified devices. The PLASMA method was unsuccessful in two of three trials with helix PCD and in all trials with the modified process challenge devices. Therefore the study indicated that EOG and LTSF systems are efficacious for simple as well as complex instruments contaminated with bacteria spores and serum.

Saito R. et al. in his letter to editor, describes an evaluation study of the efficacy of an LTSF sterilizer, Matachana LF 130 by using biological indicators (BI). A BI was placed into process challenge device (PCD) before sterilization. For the sterilization temperature of 60°C, the time of sterilization processes were 5, 10, 15, 20 and 30 min. Three BIs including *Geobacillus stearothermophilus* (ATCC7953) were used to assess sterilization: a filter paper containing $2.3 \times 10^6$ spores (SSI BI), $1.7 \times 10^6$ spores (SGM BI) and $1.9 \times 10^5$ spores (Simicon BI), respectively. An unsterilized BI was used as the positive control. The study found that cultures of the SSI BIs following 5, 10 and 15 min sterilization cycles were positive, while the cultures of the remaining yielded no growth. Bacterial growth was present in all the positive control cultures and it confirmed that the positive sample was *G. stearothermophilus*. The number of spores contained in the SSI BI was 1.4 and 12 times that of the SGM BI and the Simicon BI, respectively. This study demonstrated that sterilization temperature of less than 60°C requires a cycle time of more than 20 min. The author concluded the benefits of LTSF sterilization are efficacious, having short cycle time and safe to be used.

5.3. Cost-Effectiveness

There was no retrievable evidence on the cost-effectiveness of Matachana Low Temperature Steam and Formaldehyde Model 130 LF Sterilizer or the other brands of low temperature steam with formaldehyde sterilizer.

6.0 CONCLUSION

6.1. Safety

There was limited retrievable evidence to show that Matachana Low Temperature Steam and Formaldehyde Model 130 LF Sterilizer and other brands of low temperature steam with formaldehyde sterilizers are safe.

6.2. Efficacy
There was poor to fair level of retrievable evidence on the efficacy of Matachana Low Temperature Steam and Formaldehyde Model 130 LF Sterilizer and other brands of low temperature steam with formaldehyde sterilizer.

6.3. **Cost- Effectiveness**

There was no retrievable evidence on the cost-effectiveness of Matachana Low Temperature Steam and Formaldehyde Model 130 LF Sterilizer or the other brands of low temperature steam with formaldehyde sterilizer.

7.0 **RECOMMENDATION**

Based on the review, Matachana Low Temperature Steam and Formaldehyde Model LF 130 Sterilizer may be considered to be used in Ministry of Health hospitals for research purpose, taking into account the capacity of the sterilizer with certain provisos:

i) Whatever the process, it must result in an approved sterile product, free from hazardous levels of residues.

ii) It must be reasonably easy to use and capable of physical monitoring; at the same time have a short process time. It should be possible for the normal packaging staff to operate and control.

iii) The process should allow the product to be packaged in normal wrapping material so as not to create additional costs.

iv) It must result in a product available for immediate use.

v) It must be safe to use with standard pre-processing and have good safety margins.

However, there is a concern on the use of LTSF sterilizer which should be assessed and certified by our local environmental safety agency. This technology also needs to be certified by the necessary agency on the safety aspects, with regards to its formaldehyde concentrations, and trained authorized person who should be also certified to handle this kind of equipment. More clinical research and studies should be carried out at our various local clinical settings and validate the equipment performance since evidence showed that its efficacy can vary with different microbiological load.
8.0 REFERENCES


9.0 APPENDIX

9.1 Appendix 1

DESIGNATION OF LEVELS OF EVIDENCE

I    Evidence obtained from at least one properly designed randomized controlled trial.

II-1 Evidence obtained from well-designed controlled trials without randomization.

II-2 Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one centre or research group.

II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence.

III Opinions or respected authorities, based on clinical experience; descriptive studies and case reports; or reports of expert committees.

SOURCE: US/CANADIAN PREVENTIVE SERVICES TASK FORCE
(Harris 2001)
The additional documents provided by the manufacturer (Matachana Asia Pacific Regional Office) were mainly claims from a few published articles and laboratory test or validation report related to the efficacy and safety on LTSF sterilizer type FA 95 from Webeco, as well as in Matachana LTSF model 130 LF, which is technically identical.

Results and conclusion - summary

Efficacy:

i. A validation report on Matachana LTSF by Sterilizer Consultant Ltd. (UK) in April 2002 concluded that the LTS/LTSF sterilizer has proved to operate in a satisfactory manner when running with three low temperature steam cycles. The LTSF thermometric and microbiological test was also satisfactory over the three cycles examined.¹

ii. A test report by Webeco Test Centre & Application Laboratory (WETEC), Germany on sterilizing agent penetration in long and narrow lumens have verified full sterilization performance of Matachana/Webeco LTSF 130 LF/FA 95 at the closed end of 4 meter long thin walled PTFE-tubes, with internal diameter 1 and 2 millimeters.²

Safety:

i. Test by TUV NORD Umweltschutz GmnH & Co.Kg on formaldehyde exposure of the operating personnel when operating Matachana/Webeco LTSF demonstrated that formaldehyde concentration at the working place are well below the limiting value (< 0.5 ppm or 0.62 mg/m³), considering the average value and the short time value (peak limitation values) with 15-minutes sampling.³

ii. There was article from Central Service scientific magazine which included study by Pelaez B et al. 2003 on the detection of formaldehyde residues in plastic material sterilized in Matachana LTSF 130 LF. They found that the levels of formaldehyde detected in the different plastics following sterilization by LTSF (50°C and 60°C cycles) were below the limit proposed by the European Committee for Standardization for high risk equipment.⁴

iii. Another report from TUV NORD Umweltschutz GmnH & Co.Kg on the examination of water tests on formaldehyde concentration of Matachana/Webeco LTSF indicated that the concentrations clearly below limit values (0.5 g/L to 20 g/L).⁵

Other related information:

i. Another article from Central Service scientific magazine included study by Gaspar MC et al. 2002 on microbiological efficacy of Sterrad 100S and LTSF sterilization systems compared to Ethylene Oxide. In conclusion, LTSF (both cycles) was the most efficacious method, and was the only method unaffected by the presence of salt. In the absence of salt, all methods showed similar efficacy.⁶
ii. More recently, Pelaez B et al. 2007 conducted a study of environmental levels of formaldehyde emitted by a LTSF sterilizer in the Hospital San Carlos, Madrid, Spain. The results of this study suggested that indoor air formaldehyde concentrations were very low and complied with international regulation.7

Based on the additional document provided by the manufacturer, there was still inconclusive and insufficient of high quality scientific evidence to demonstrate the efficacy and safety of Matachana LTSF 130 LF. Evidence quality can be assessed based on the source type (from meta-analyses and systematic reviews of triple-blind randomized clinical trials with concealment of allocation and no attrition at the top end, down to conventional wisdom at the bottom), as well as other factors including statistical validity, clinical relevance, currency, and peer-review acceptance.

Recommendation
Matachana LTSF sterilizer model 130 LF still can be recommended to be used in MOH hospitals as a research tools in research environmental in order to provide more quality scientific evidence.

References
  3. Kahre C. Expertise on formaldehyde exposure of the operating personnel when operating the LTSF – sterilizer WEBECO FA95/Matachana 130 LF