LivaNova
Health innovation that matters

March 2019

Frequently Asked Questions (FAQs) Update regarding the 3T Heater-Coolers with Vacuum & Sealing design upgrade

Valid Outside of the United States Only

In this document, questions and related answers are divided in chapters, according to reference topics, as follows:

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Vacuum & Sealing Upgrade

1. ***Q: What does the 3T[2] Heater-Cooler Vacuum & Sealing Upgrade consist of?***
   A: The 3T Heater-Cooler Vacuum & Sealing Upgrade ("3T V&S Upgrade") consists primarily of a modification of the 3T design to include improved internal sealing and addition of a vacuum system to new and existing devices. These changes are intended to further reduce the risk of possible dispersion of contaminated aerosols from the 3T Heater-Cooler devices in the operating room.

2. ***Q: How is the*** **''3T Heater-Cooler Vacuum & Sealing Upgrade'' (3T V&S Upgrade) addressing the issue of aerosolization?**
   A: The 3T V&S Upgrade solution is capable of collecting and sequestrating aerosol from the 3T Heater-Cooler device (3T HCD) and preventing it from entering into the sterile field.

[1] LivaNova PLC is a U.K. holding company with a number of wholly-owned subsidiaries, including LivaNova Deutschland GmbH. In this document, we refer to all entities using the brand name LivaNova.

[2] The 3T is a non sterile heating-cooling machine manufactured by LivaNova Deutschland GmbH. It is used to control patient's body temperature over a cardiopulmonary bypass procedure.

3. ***Q: How can the 3T V&S Upgrade prevent aerosols from being dispersed in the OR?***
   A: The 3T V&S Upgrade solution includes the application of a vacuum solution capable of connecting the 3T HCD to a vacuum source (i.e. central hospital vacuum source or stand-alone vacuum source) and the regular use of a disposable suction canister with an antibacterial filter (Aerosol Collection Set).

   The disposable set is intended to (i) receive the water that might overflow from the tanks when the water contained in the external circuitry is returned in the tanks at the end of the CPB procedure (just like the overflow bottle before the V&S design change), and (ii) collect and segregate any aerosols generated by the agitation of the water in the tanks when the 3T is switched on.

   The collection of aerosols is achieved by the airflow generated by the pressure difference between the inside of the tank and the suction canister connected to the vacuum source. The sequestration of any aerosol is achieved by the antibacterial filter located at the outlet port of the suction canister before the vacuum source.

4. ***Q: Is the 3T V&S Upgrade approved in all countries?***
   A: LivaNova has obtained CE mark for ''3T V&S Upgrade,'' in May 2017 and has been working with local competent authorities to obtain approval for this solution in each country. The company started the roll-out of these design upgrades on a global basis in July 2017, and has is progressing with the update, as we obtain approval by local regulatory agencies. Timeline for clearance may significantly vary country by country, therefore implementation has almost completed in some regions, while in some other countries has still not started.

5. ***Q: Who will pay the costs for the installation of the 3T V&S Upgrade?***
   A: The installation of the 3T V&S Upgrade is performed by LivaNova at no cost to our customers.

6. ***Q: Can I perform the disinfection less frequently once my 3T device is upgraded?***
   A: No, the routine maintenance of the device will continue to be a key measure to ensure the water inside the tank remains clean.

7. ***Q: Are all 3T devices be eligible for the 3T V&S Upgrade?***
   A: Yes. All 3T devices currently present in the field will be eligible to receive the 3T V&S Upgrade, regardless of their manufacturing date or whether or not the device has shown evidence of contamination. It is possible that some devices may not be able to receive the 3T V&S Upgrade as a result of age, condition from lack of maintenance, or other factors. In such cases, we will work with your facility on an alternative solution.

8. ***Q: Is the 3T V&S Upgrade solution available also for 1T devices?***
   A: The 3T V&S Upgrade is not currently available for 1T devices. Please refer to section '' *End of service for 1T devices''* for other question related to 1T

Aerosol Collection Set

9. ***Q: What is the 3T Aerosol Collection Set?***
   A: The 3T Aerosol Collection Set (the disposable components of the 3T V&S Upgrade) consists of a suction canister, a suction canister lid and two pieces of tubing; the longer piece of tubing includes a 90° connector for connection to the vacuum port on the lid of the canister.

10. Q: How can I order the 3T Aerosol Collection Set?

A: The disposable to be used as part of 3T V&S Upgrade can be ordered from LivaNova by means of the following item:

- 3T Aerosol Collection Set Item 050900100 (12 units per box)

At the time of the 3T V&S Upgrade on 3T HCD already in the field, LivaNova will ship to each customer, for each 3T unit to be upgraded, one case of 3T Aerosol Collection Sets (containing 12 units) at no cost, to ensure that every 3T device is covered for the first calendar month.

To cover the second calendar month and beyond, customers should start ordering 3T Aerosol Collection Set on a regular basis from LivaNova Customer Service.

Depending on the layout of the OR, in case the 3T HCD is more than 3,5 mt away from the vacuum source, customers may need to order an additional extension line (366 cm)

- ¼" ID vacuum extension line with connector, 366 cm (12 ft) Item 050900111 (50 units per box)

It is expected that only a limited number of hospitals will need the ¼" ID vacuum extension line with connector, therefore this item will not be shipped automatically at the time of the 3T V&S Upgrade, but will have to be ordered, if needed.

The above is valid only for upgraded machines. For new 3T HCD ordered to LivaNova, customers should start ordering 3T Aerosol Collection Set on a regular basis from LivaNova Customer Service.

11. Q: Can I use a different canister already present in the hospital?

A: LivaNova has validated the 3T V&S Upgrade as a system using a specific canister and tubing. We cannot guarantee that the use of an alternate disposable could provide an effective prevention against possible aerosol emission.

12. Q: When should the Aerosol Collection Set be replaced?

A: As per 3T Aerosol Collection Sets Instructions for Use, after 3 calendar days of installation, the Aerosol Collection Set has to be replaced and discarded.

13. Q: Which kind of vacuum source is recommended? Are there specific requirements?

A: The use of a central hospital vacuum source is recommended for use with this disposable. The vacuum source must be capable of 20 l/min flow or greater.

14. Q: If a central vacuum source is not available in the OR, what are my options?

A: If a central hospital vacuum source is not available the use of a portable vacuum system capable of 20 l/min flow per ISO 10079-1 for Medical Suction Equipment is required. The portable vacuum source must be specified for medical applications and fulfill the requirements of IEC 60601-1 and IEC 60601-1-2.

15. Q: Is LivaNova selling the portable vacuum system?

A: No. LivaNova is not selling the portable vacuum system but we have identified a suitable device that meets all requirements. Please contact your local sales representative for more information about this possible option.

Deep Disinfection

16. Q: What is the deep-disinfection (DD) service?

A**:** The deep-disinfection (DD) service is a special service implemented by LivaNova in 2015 that allows facilities to return heater-cooler units for a full cleaning, disinfection

and replacement of connectors and tubing. The DD service is currently implemented at LivaNova facilities in Munich for all markets outside of USA. Since its availability, the DD service has been frequently used by European facilities that knew or suspected contamination of their heater-cooler devices.

17. Q: How long does it take for a DD service?

A: The complete DD process requires a minimum of 10 starting from when the unit is returned to LivaNova to when the unit is back to the hospital.

18. Q: Under which conditions can a confirmed M. chimaera contaminated unit access DD service?

A: As global leader in the heater cooler market, LivaNova is committed to both helping clinicians and institutions ensuring the continued use of our heater cooler devices, which are recognized as playing a critical role in the cardiac surgery OR around the world. Until June 2020, the deep disinfection service will be made available at no cost to all facilities requesting it who will demonstrate to have a confirmed M.chimaera contaminated unit. While submitting your request for a DD service at LivaNova, you will be requested to file an official complaint to LivaNova and provide documentation to confirm the M.chimaera contamination according to your facility's testing protocol.

19. Q: Will LivaNova provide a loaner for all units undergoing a DD?

A: A loaner request can be submitted to LivaNova, and will be evaluated. Absolute priority for the DD service as well as for a potential loaner will be given to units with a confirmed for M. chimaera contamination. Until June 2020, there will be no charge for the approved 3T loaner device, shipping, installation or service, when related to units with confirmed M. chimaera contamination.

20. Q: In cases where additional units are contaminated with M. chimaera at the same facility, will LivaNova provide multiple loaners?

A: To ensure we can maximize the number of hospitals we can serve at the same time, we will allocate a maximum of one loaner device per institution. In case an institution has more than one device contaminated with M. chimaera, a rotation mechanism should be implemented. Once the first device is returned to the hospital after DD, a second device can be shipped to LivaNova for DD. When all devices will have completed DD and the last will be returned to the hospital, the loaner will have to be returned immediately to LivaNova. More than one loaner might be allocated at the expense of the customer, depending on availability.

21. Q: Can contaminated units not confirmed for M. chimaera access the DD service?

A: It is our goal to guarantee access to the DD service to all our customers, and therefore facilities who have contaminated units, but not confirmed to be M. chimaera contaminated, can certainly request a DD service. These units will be charged a fixed minimum fee. While submitting your request for a DD service at LivaNova, you will be requested to file an official complaint to LivaNova and provide documentation to confirm the contamination, according to your facility's testing protocol.

22. Q: How can I submit to LivaNova a request for DD and for a loaner?

A: You may submit your DD request by contacting your LivaNova sales representative.

23. Q: How long does it take to perform a test for M. chimaera?

A: It may take a maximum of 8 weeks

24. Q: Is LivaNova providing a protocol for testing for M. chimaera?

A: LivaNova will not provide a specific protocol for testing for M. chimaera. Each institution is free to apply their own testing protocol.

25.Q: What are the limitations for devices suitable for Deep Disinfection (DD) Service?

A: The production date and age of the device is important for successful deep-disinfection service.

- Typical average useful lifetime of medical device equipment is ~10 years.
- Devices less than 10 years old are usually suitable for deep-disinfection, depending on the condition of the device
- Devices more than 10 years old may not be suitable for deep-disinfection.
    - The overall condition of older devices generally requires additional repair work which is not included in the deep-disinfection service and would be subject to significant additional charges to the customer
    - Design changes
    - The feasibility of performing a successful DD on a device older than 10 years will have to be evaluated case by case by a LivaNova Authorized Service Technician on site, as further significant costs may occur when aiming to restore functional capability of the device.
- When units will be returned for DD, all potential additional costs, i.e. repairs needed to restore functional capability of the device, will be submitted to customers for pre-approval before proceeding with further steps.
- Repairs necessary to restore functional capability of the device will be charged unless under warranty
- Customers will provide the decision whether to proceed with repairs to restore functional capability or other options (e.g. buy a new device).

- NOTE: Heater-coolers produced before 2007 are not suitable for the deep-disinfection process for the points above mentioned

26.Q: How do I know when my 3T heater-coolers were manufactured?

A: All 3T heater-coolers have a label affixed to the back panel of the device showing the serial number (beginning with 16S-) and date of manufacture.

NTM infections risks in Cardiac Surgery

27.Q: What information is known about the potential risk of NTM transmission at this time?

A: LivaNova has previously conducted, and is continuing to conduct, extensive testing and data collection to understand how NTM transmission may be occurring during the use of heater-cooler devices. In this process, the company has consulted numerous experts to understand this phenomenon. The current thinking of the company is as follows:

- The failure to clean and disinfect a water circuit of a heater/cooler can allow biofilm formation. NTM is known to proliferate in biofilm and may lead to contamination of the heater/cooler water circuit.
- In operation of the device, air bubbles may be generated in the water tanks and then exit the device as aerosolized particles. The NTM present in the water may be carried by aerosolized particles out of the tank.
- Via air flow, the aerosolized particles may then be dispersed into the surrounding environment.
- The state of scientific knowledge provides no evidence that NTM can be transmitted via water evaporation because individual water molecules formed by evaporation are too small to carry the bacteria.

The literature currently available highlights that a key consideration with potential NTM transmission is the nature of the organism at issue. NTM is a ubiquitous environmental contaminant that is present in many water supplies, in the air, and in other non-sterile environments. NTM is also frequently identified in hospital environments. Consequently, in a non-sterile environment, such as outside of the sterile field of an operating room,

NTM can certainly be present. NTM presence can result in post-surgical infection only if directly transmitted to the patient.

LivaNova's heater-coolers are cleared by Regulatory Bodies as a non-sterile device. Like other equipment used outside of the surgical field during open-heart procedures (such as anesthesia machines and pharmacy carts, for example), heater-coolers are not sterile and cannot practically be used in a sterile fashion. Sterility of the water circuit during device operation is also not possible, as the devices are operated and maintained in non-sterile environments. Furthermore, since the LivaNova heater-cooler's water circuits are physically separated from the blood circuit and are not intended to come into contact with this circuit, it is not necessary for the water circuit to remain sterile. The periodic cleaning and disinfection procedures described in the device's Operating Instructions are intended to control biofilm formation and bacterial growth.

28. Q: What further investigation has LivaNova done to understand this issue?

A: Since the company became aware of this issue, the company has proactively conducted an investigation into the issue of potential NTM infection, and has had ongoing conversations with numerous government regulatory agencies. It is important to note that the initial report received by the company in 2014 described airborne NTM, a phenomenon that had not been previously known to either the company or the scientific or physician community. The company undertook an intensive investigation into how this might occur, essentially creating new knowledge to understand the phenomenon. This investigation has resulted in the company's current thinking about how NTM may become aerosolized and dispersed. Our investigation work continues in close collaboration with Competent Authorities.

29. Q: What has LivaNova done up to now to respond to this potential risk of infection?

A: LivaNova has taken the following actions, among others, in its investigation and response:

- **Device Manufacturing and Design Changes**
  - The company implemented a post-production/pre-shipment disinfection process at the production facility in mid-August 2014 to supplement the pre-existing cleaning and disinfection process in the field.
  - The company implemented additional manufacturing measures to mitigate the risk of NTM (e.g., drying process, disinfection of production equipment, use of PALL-filtered water, monitoring for NTM presence at certain points of the manufacturing process, and hot disinfection of water basin of pump assembly area).
  - The company implemented design changes for devices in production (e.g., replacing device tubing, plugging unused overflow outlet).
  - LivaNova continued to work with regulators to develop a broad-scale solution to further mitigate the already low risk of NTM transmission, and ensure continued clinician access to this important device which enables lifesaving cardiac surgery. In May 2017, the company achieved CE mark for the Vacuum & Sealing design solution upgrade and started soon after its roll-out on all 3T HCDs on global basis, progressing with implementation as local approvals become available.
  - Starting from December 2018, LivaNova has implemented to its 3T HCD series production, for the markets where these changes are approved by

local Regulatory Bodies, all design changes introduced on the devices already in the field by means of Field Safety Corrective Actions from 2015

- **Device Labeling**
  - In June 2015, LivaNova initiated a Field Safety Correcting Action, informing all customers on world basis about a newly identified risk associated with NTM infections in cardiac surgery and importance of continuing to adhere to the cleaning and disinfection process. LivaNova contacted all its HC customers globally to remind users the importance of following the company's disinfection and maintenance procedures, inform customers that bacteria may become aerosolized during H/C operation, serving as a source for contamination, provide customers with updated operating instructions regarding disinfection and maintenance procedures.

  - The company has also provided information to customers regarding how to handle devices suspected of contamination and how to conduct environmental monitoring.

  - LivaNova's Operating Instructions for the 3T System have included instructions for cleaning and disinfection as long as the device has been commercially distributed. Failure to perform adequate cleaning and disinfection per the Operating Instructions has the potential to lead to contamination, including NTM contamination. As more information has become available and while our investigation is ongoing, the device's cleaning and disinfection regimen has been revised to require: more frequent disinfection of the water circuit (e.g., disinfection every two weeks rather than quarterly) with specified disinfectant solutions; weekly water changes; and the addition of hydrogen peroxide solution to the water to act as a preservative and to further prevent biofilm formation.

  - Updated operating instructions have been distributed in June 2015 as part of a FSN issued to all 3T System users globally. Since 2015, LivaNova has issued different Field Safety Notices to provide additional instructions for the users in relation to potential Nontuberculous Mycobacteria (NTM) contamination Risk.
  - In March 2019, LivaNova has released and will be distributing a new revision of the Operating Instructions that is applicable to all 3T devices already equipped with the vacuum and sealing design solution. The new Operating Instructions will consolidate the content of the previously released Field Safety Notices.

- **Device services**
  - In 2015, LivaNova implemented a deep-disinfection service available within the European Union by which facilities can return the HCU for a full cleaning, disinfection and replacement of connectors and tubing. This service has been frequently used by facilities that observed or suspected contamination of their devices.

  - In 2018, the deep-cleaning service has been implemented also in the USA, to serve the units present in the US market.

30.Q: What other recommendations does LivaNova have regarding use or maintenance of the device?

A: LivaNova believes that patient safety requires a shared partnership between LivaNova and users of the 3T heater-cooler. LivaNova takes care in manufacturing the

3T heater-cooler and in providing comprehensive Operating Instructions to customers. To help ensure correct functionality, safety and cleanliness of the 3T heater-cooler and to further minimize risk to patients, the user must also perform the specified routinely required tasks – these include cleaning and disinfection of the device before initial use of the 3T heater-cooler device and thereafter as indicated by the Operating Instructions, as well as regular maintenance checks. Depending on the nature of the service, these maintenance checks can be performed by LivaNova technicians or trained hospital personnel.

31. Q: Who do we contact if we want to report a complaint or have questions about the 3T heater-cooler generally?

A: LivaNova has an established system for receiving and processing any relevant information regarding complaints and evaluating any potential adverse events. Customer complaints can be received by LivaNova's Sales Representatives or Field Clinical Representative or Technical Service Representative. LivaNova encourages reporting of complete information, so field experiences can be adequately evaluated and investigated.

For general technical or service questions related to the LivaNova heater-coolers, please continue to call your local contact within LivaNova Sales or Field Clinical or Technical Service organizations.

Compatibility with certain oxygenators with polymer heat exchanger designs

32. Q: Which conditions were used for INSPIRE tests?

A: LivaNova has performed in vitro testing using water (worst case situation) and bovine blood for the evaluation of hydrogen peroxide diffusion across the Inspire heat exchanger polymer fibers. The conditions used in these tests consisted of circulating water or bovine blood on the patient side of the CPB circuit simulating different patient body weights and H2O2 at a concentration of 330 ppm in the 3T heater-cooler water circuit for a duration of 6 hours.

33. Q: What is the H2O2 permeability rate of INSPIRE and what is the safety factor vs. the AL?

A: The quantity of hydrogen peroxide transferred from the water side to the blood circuit an adult patient of 60Kg connected to an Inspire oxygenator was found to be 57 times below the Allowable Limit (AL) for daily systemic exposure to hydrogen peroxide.

34. Q: Will LivaNova provide an official Dear Customer Letter on INSPIRE permeability rate to be delivered to your customers?

A: Yes, an official customer letter is available for customer distribution and can be downloaded from the 3T Heater-Cooler section of the LivaNova web site at: https://www.livanova.com/en-GB/Home/Products-Therapies/Cardiovascular/Healthcare-Professionals/Cardiopulmonary/Heart-Lung-Equipment/3T.aspx

35. Q: Do you have a comparison of all oxygenators (including third parties) tested in the same conditions?

A: Yes, we have performed tests with several oxygenator models, including third parties oxygenators which confirmed variable permeability of the heat-exchangers depending on their design and construction.

36. Q: Which third party oxygenators are non-compatible with the 3T instructions for use?

A: Declarations of compatibility for third party oxygenators should be requested to and provided by the manufacturer of the devices of interest. LivaNova cannot guarantee the

compatibility of technical features and/or device performances that are not specified by the manufacturer.

37. Q: How do you explain that different oxygenators (all with polymer HE) have different behaviors in terms of diffusion?

A: Heat Exchanger design, manufacturing process and fiber characteristics may all play a role with respect to diffusion through the HE fibers. We do not have access to these data for competitive device for us to be able to understand the variability observed from one device to the other one

38. Q: Why is 3T requiring disinfection every two weeks, addition of H2O2 as a preservative between two disinfection cycles and H2O2 daily monitoring, while other H/C are much less demanding and do not need to add any preservative?

A: Our tests have demonstrated that even if you fill a clean tank with filtered water, the number of microorganisms present is going to grow (because neither the tank not the water are sterile just as what we have in a heater-cooler) and they will develop biofilm over time. The hydrogen peroxide is acting as a preservative limiting the development of the microorganisms and preventing biofilm formation. The longer is the time interval between water changes and disinfection, the more is the need to use something to control the microorganism development.

Hydrogen Peroxide Concentration

39. Q: Does the daily hydrogen peroxide level monitoring process mean the disinfection process does not work?

A: No. LivaNova Deutschland GmbH has defined a procedure to maintain the water quality in the Heater-Cooler device at drinking water level. The procedure in the 3T Operating Instructions specifies that the water circuit has to be disinfected with certain disinfectants before first use and then every two weeks. To maintain the water quality, 150 ml of medical grade 3% hydrogen peroxide ($H_2O_{2)}$ must be added to the filtered tap water used to fill the tanks every 7 days. The purpose of adding the hydrogen peroxide is to limit microbial growth between the regular disinfection cycles performed every 14 days. The implementation of the daily hydrogen peroxide level monitoring process does check the effectiveness of the hydrogen peroxide preservation over a 7 day period but does not mean that the current disinfection is not effective.

40. Q: If my device has been upgraded with the Vacuum & Sealing (V&S) Upgrade Solution do I still need to follow the daily hydrogen peroxide monitoring process?

A: Yes, the V&S upgrade solution prevents the release of aerosols from the 3T device and thus reduces the risk of patient infections caused by air transmissions. But the V&S upgrade solution does not mitigate the risk related to direct water contact. Therefore, it is important to maintain the water quality at drinking water level to prevent any nosocomial infections caused by direct water contact. Consequently, it is important to monitor the effectiveness of the water preservation.

41. Q: Why is LN just now communicating / addressing this corrosion and hydrogen peroxide level issue?

A: LivaNova performed a confirmatory validation of the efficacy of the water preservation solution (addition of hydrogen peroxide). The results of the tests

performed have confirmed that water preservation solution is effective in limiting the growth of micro-organisms on new machines. However, the efficacy was not confirmed on some clinically-aged devices. Our investigation revealed that copper was exposed if the nickel coating corroded off the evaporator coil. The copper interacted with the hydrogen peroxide and reduced the effective concentration. Therefore an increase in microbial counts (HPC) over the 7 days operating period was observed, and was above the specification of 100 CFU/ml.

42. Q: Why do the cooling coils degrade over time?

A: To support optimum heat transfer the 3T device uses nickel-plated copper cooling coils in the Patient and Cold Cardioplegia tanks. The cooling coils are constantly submerged in a mixture of filtered tap water and different chemicals (Hydrogen Peroxide or Disinfectants). When the device is operated, this fluid is subjected to temperatures cycles (heating and cooling) and fluid flow streams generated by the internal pumps within the water tank. In this working environment multiple degradation processes can take place (e.g. galvanic corrosion, disinfectant chemical corrosion, erosion and mechanical stresses). In some cases, the combination of these phenomena can lead to a progressive degradation of the cooling coil over time.

43. Q: I have an older device; does this mean I have a degraded cooling coil? Will LN replace my coil?

A: Degradation of the cooling coil will occur over time and is dependent on the frequency of use and the frequency of chemical disinfections. Older devices will typically show more degradation versus newer devices. LivaNova will not replace the cooling coil unless under warranty.

44. Q: Can I visually inspect my device to determine if I have a degraded cooling coil? If my cooling coil is not degraded do I still need to follow the new daily hydrogen peroxide process?

A: To avoid possible damage to the 3T device, inspection of the cooling coils must be performed by a certified service technician. Inspection can be done by either disassembling the device or by means of an endoscope inserted into the temperature probe openings located on top of the 3T tanks. Even if the cooling coil is not degraded it is important to follow the daily monitoring of the hydrogen peroxide concentration in order to maintain the effectiveness of the hydrogen peroxide as a water preservation method.

45. Q: What is LN doing to address/stop the cooling coil erosion?

A: The stirrer pump that is located in the 3T patient tank is replaced with a new design as a part of the overall 3T sealing upgrade and vacuum solution. This design upgrade to the stirrer pump will reduce the rate of surface erosion of the cooling coil caused by the flow stream originating from the stirrer pump.

46. Q: Do I have to perform daily monitoring on devices that are not going to be used that day?

A: Yes, you should monitor the hydrogen peroxide levels on days when the device is not in use and take the actions recommended in the Operating Instructions to prevent an increase in microbial growth during the time period the machine is not in use. If the device will not be monitored for more than a day (e.g. over a weekend), the device must be completely drained.

47. Q: How was the hydrogen peroxide 100 ppm guide developed/established?

A: In 2011, at the recommendation of a water hygiene expert , the company revised the 3T Operating Instructions to include steps to achieve water quality that meets the standard for German drinking water (≤100 CFU/ml). These changes included the

addition of hydrogen peroxide to the water as a preservative. During verification testing of the preservation it was observed that hydrogen peroxide levels above 100 ppm kept the water within the specified drinking water limit.

48. Q: What make and model of test strips do I need to use for the hydrogen peroxide testing, and can I use other test strips not mentioned in the FSN?
A: The concentration in the water can be measured semi-quantitatively by visual comparison of the reaction zone of a test strip (e.g. MQuant, Peroxide Test, Method: clorimetric with test strips, 100-1,000 mg/l H2O2, Reference 1.10337.0001) with the fields of a color scale. Other commercially available colorimetric test strips that provide a 100 - 1,000 mg/l H2O2 range of testing are acceptable

49. Q: Where can I purchase the H2O2 test strips?

A: H2O2 concentration test strips are available from various laboratory supply websites such as

- EndoSan (https://www.endosan.com/product/endosan-high-range-0-1000ppm-hydrogen-peroxide-test-strips-100-strips)
- Johnson / J-QUANT®Peroxide 1000 (http://www.johnsontestpapers.com/products/J-QUANT/product/Peroxide)
- PLPrecision (https://preclaboratories.com/product/peroxide-test-strip-400ppm)
- Macherey-Nagel QUANTOFIX Peroxid 100,CE 705

50. Q: What do I have to do with my 3T units on days when there are no cases (i.e. weekends)?
A: If the 3T heater cooler is not intended to be used for more than a day, you may monitor the hydrogen peroxide level on days when the machine is not in use. Alternatively, if the device will not be used or monitored for more than a day (e.g. over a weekend), the device must be completely drained. For long term storage of the heater-cooler refer to Section 6.5 of the Operating Instructions, Preparing the heater-cooler for storage.

51. Q: At what point can I stop testing the hydrogen peroxide levels?
A: If the device is not used for more than a day (e.g. over the weekend), the device must be completely drained. At this time the monitoring can be stopped until the device is brought back into service. For long term storage of the heater-cooler refer to Section 6.5 of the Operating Instructions, Preparing the heater-cooler for storage.

52. Q: If I cannot keep my hydrogen peroxide level at the required ratio, does it mean my machine is damaged?
A: Frequent addition of hydrogen peroxide is an indication that the cooling coil is degraded. However, this does not indicate that the machine is damaged and unable to function. If the reaction zone of the test stripe shows hydrogen peroxide concentrations below 100mg/l H_2O_2, add an additional 100ml of medical grade 3% hydrogen peroxide to the water tanks as described in chapter 6.4.2 ''Monitoring and adjusting the hydrogen peroxide concentration'' This will limit the bacteria growth at an acceptable level. Daily monitoring of hydrogen peroxide concentration levels should allow you to maintain the required ratio.

53. Q: Will this negatively impact the functionality and/or reliability of my device?
A: Frequent addition of hydrogen peroxide is an indication that the cooling coil is degraded. However, this frequent addition does not indicate that the machine is damaged and unable to function.

54.Q: If my hydrogen peroxide test does not meet the minimum level and I drain and refill the device (with water and hydrogen peroxide), do I need to test the hydrogen peroxide level again before putting the device back into service?
A: Yes, hydrogen peroxide concentration should be tested every day in each of your devices. If the 3T heater-cooler is not monitored daily for hydrogen peroxide concentrations, drain the water tanks. Hydrogen peroxide concentration testing should be performed prior to using the device in a procedure. Please refer to chapter 6.4.2 ''Monitoring and adjusting the hydrogen peroxide concentration''

55.Q: If I cannot get my hydrogen peroxide levels above the minimum, can I continue using my device?
A: Yes. Please refer to chapter 6.4.2 ''Monitoring and adjusting the hydrogen peroxide concentration'' in the Operating Instructions.

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56.Where can I find the instructions to position the 3T HCD for clinical use?
A: Chapter #4 contains the operating instructions for installation. Paragraph 4.2.1 ''Placing the heater-cooler'' indicate how to position the 3T HCD in relation to both the exhaust vent system of the operating theatre and the operating table

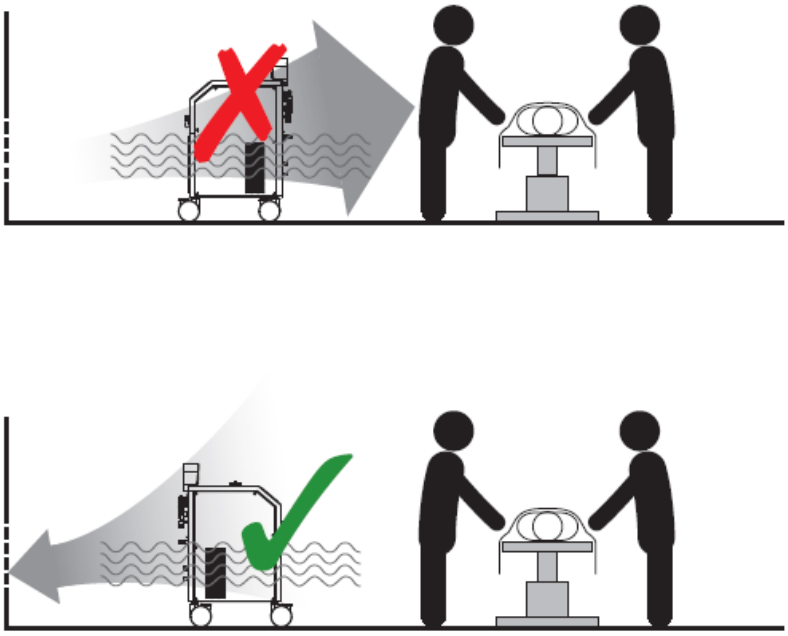

Fig. 4: Placing the heater-cooler in relation to the exhaust vent system

57.Q: Where can I find all instructions for routine maintenance of the 3T heater-cooler device
A: Chapter 6 contained the Routine maintenance operating instructions

58.Q: Is there a summary of the timelines for routine disinfection and related tasks?
A: Yes. You can find the summary table in paragraph 6.1.2. Please find it here below

6.1.2 Timelines for disinfection and related tasks

Time / Interval	Task	For details refer to ...
◗ every day prior to using the heater-cooler	→ check and, if necessary, adjust the H_2O_2 concentration in the water tanks	chap. 6.4.2
◗ prior to initial operation ◗ prior to storing the heater-cooler	→ disinfect the surfaces and water circuits	chap. 6.2 and chap. 6.3
◗ after every operation	→ disinfect the surfaces	chap. 6.2.1
◗ greater than 7 days of use	→ change the water if in use greater than 7 days; add hydrogen peroxide to the tanks	chap. 6.4.1
◗ after the allowed use period stated in the separate instructions for use delivered with the disposable	→ replace the 3T Aerosol Collection Set	separate instructions for use for disposable
◗ every 14 days (also applies for systems in storage)	→ disinfect the water circuits	chap. 6.3
◗ once a month (before and after disinfecting the water circuits)	→ monitor the water quality for total bacteria count	chap. 6.3.3
◗ every 6 months (before and after disinfecting the water circuits)	→ monitor the water quality for NTM	chap. 6.3.3
◗ once per year	→ replace the tubings used with the heater-cooler	chap. 6.7

59.Q: Are there videos on the routine maintenance steps required?

A: Videos referred to the updated operating instructions for several key sections of the manual are planned to be released and uploaded on the 3T LivaNova website page, out of USA section

60.Q: Is there a list of approved pre-soaked disinfection wipes?

A: Yes. You can find the list in paragraph 6.2.1

6.2.1 Cleaning and disinfecting the device surfaces

List of approved pre-soaked disinfectant wipes

Product name	Manufacturer
Bacillol AF Tissues	Bode (Hartmann)
CaviWipes *	Metrex
Mikrozid AF Wipes	Schülke & Mayr
Sani-Cloth Active Wipes +	PDI

* available in the USA
+ available in Australia

61.Q: Is there a list of approved disinfectants?

A: Yes. You can find the list in paragraph 6.3.1

List of approved disinfectants

For disinfection of the water circuits, use Puristeril 340, Peresal, Minncare Cold Sterilant, Clorox Regular Bleach 1 or another LivaNova-approved disinfectant.

Product name	Manufacturer	EPA Reg. No.
Puristeril 340	Fresenius Medical Care	
Peresal	Ecolab	
Minncare Cold Sterilant	Minntech Corporation	52252-4
Clorox Regular Bleach 1 (active ingredient: 8.25% sodium hypochlorite)	Clorox Company	5813-100

62. Q: Where can I find the operating instructions related to water quality monitoring? What are the monitoring required and what is the frequency?

A: Please refer to paragraph 6.3.3 for detailed instructions on water quality monitoring. It is required to monitor:

- the quality of the water in the tanks at least once a month before and after disinfecting the water circuits
- it is recommended to check the water quality for NTM every 6 months before and after disinfecting the water circuits

63. Q: What are the specified microbial counts limits that must not be exceeded?

A: Please refer to paragraph 6.3.3 for detailed instructions on water quality monitoring. The limits are set as follows:

- Total bacteria counts must not exceed the limit of 100CFU/ml
- NTM must not be detectable in 100 ml (< 1 CFU/100 ml)

64. Q: What to do if the microbial counts exceed the specified limits?

A: Please refer to chapter 6.3.3 for detailed instructions on water quality monitoring. ‘’If the microbial counts exceed any of the specified limits, please contact your hygiene officer and your authorized service technician for a root cause analysis and the respective measures to be taken (e.g. a deep disinfection service offered by LivaNova)’’

Evidence of effectiveness for measures introduced by LivaNova

65. Q: Has LivaNova developed and conducted specific tests to confirm that the V&S upgrade solution is effective?

A: Yes. LivaNova has developed, documented and executed various microbiological testing to confirm that the Final Configuration of the 3T HCD system connected to a vacuum source through the 3T Aerosol Collection Set is effective in preventing airborne transmission of non-tuberculosis mycobacterium (“NTM”) potentially emitted from the device over a specified range of negative pressures in various operating conditions. Tests were performed at accredited 3rd party laboratories specialized in aerosol emission testing.

66. Q: Which testing conditions have been applied to represent the worst case scenario?

A: The studies were conducted using a well-controlled test chamber with highly contaminated devices that were inoculated with a high load (1x106 CFU/ml) of M. Chimaera as a worst-case scenario. Aerosol sampling occurred at two specific phases

for each device: warming (in which the water temperature was increased from 18°C to 40°C) and emptying of the external water lines. These two test conditions represent worst case aerosol emission events due to the driving forces applied, heating the water and return of water to the HC3T tank from the water circuits.

67. Q: What results have been obtained?

A: The test results do demonstrate that the HC3T Vacuum & Sealing Solution significantly reduce M. Chimaera aerosolization when compared to the Not Upgraded 3T HCD for both percentage reduction and logarithmic reduction. The studies show that the Vacuum & Sealing solution is effective in mitigating aerosolized M. Chimaera emission, with a greater than 3 Log10 when compared to the Non-upgraded HC3T devices for all test conditions. In percentage terms, this means a greater that 99,9% reduction

68. Q: Which size of particles has been considered by LivaNova in its testing?

A: Aerosol Particle Size (APS) Testing was conducted considering the following

- NTM are rods with diameter 0.3-0.5 mm, length 1.5-4 mm[1]
- Consulting and regulatory body microbiologists indicated that aerosols of size 0.3-5 mm are likely to contain NTM[1]
- LivaNova testing includes all particles >0.3 mm

It is to be noted that competitor product literature does not report results for < 5 mm size aerosol particles[2] and does not report worse case conditions considered in the tests conducted to demonstrate efficacy of design solution

Sources:

1. LivaNova FDA supplemental submission S021 of Q160637
2. Competitor data published March 2017
3. LivaNova data on file, MRIGlobal testing (May 15, 2018)

End of service 1T devices

69. Q: What is the End Of Service date for 1T devices?

A: The end of service for all 1T devices occurred on December 31st , 2018. Starting January 1st, 2019 LivaNova does not provide any longer service activities for 1T devices, including preventive maintenance.

70. Q: What is the impact of End of Service to customers?

A: As stated in the Operating Instructions, paragraph 6.1.2, according to applicable regulation**s** and standards**,** LivaNova had determined that a preventive maintenance check for the Heater-Cooler 1T must be carried out either after every 1000 operating hours or every 12 months, whichever is the earlier. The preventive maintenance activity can be performed only by a LivaNova authorized person.
As communicated to customers globally, from January 1st, 2019 LivaNova does not provide any longer service activities including preventive maintenance. As the preventive maintenance by a LivaNova authorized representative is a mandatory requirement to operate the device this means that the machines shall be put out of service within 1 year or 1000 hours from the last preventive maintenance

71. Has this been communicated to customers?

A: Yes. In May 2018 LivaNova issued and sent a Dear Customer Letter to all its customers globally to inform about the end of service date and its implications.