

October 2015

Dear Valued Customer,

We would like to provide you with an update on what Sorin has done since we were made aware of a mycobacteria contamination issue involving our 3T heater-cooler. This update includes measures we are currently taking to further lower the risk of emission in the operating theatre while reducing the effort and workload for your team. We are devoting all necessary resources to achieve these results, including working with a multidisciplinary team that includes external microbiology experts.

Our investigation has shown that contamination by mycobacteria is a general problem affecting all heater-coolers used in the operating room and is not restricted to Sorin heater-coolers. This has been further confirmed by a recent communication issued by the FDA in October 2015.¹ To date, Sorin is the only company that has provided specific instructions to mitigate the risk of infection. We have also offered a deep disinfection service to users with contaminated devices. Based on these improvements, we are assuring Sorin customers that they may continue to safely use the Sorin heater-cooler.

Below is a detailed summary of the actions Sorin has taken and the measures we have implemented:

January 2014 – Sorin was informed of a newly identified risk

- Sorin was made aware of cases of non-tuberculous mycobacteria endocarditis—or deep infection—following open heart surgery during which a heater-cooler device was used. In few rare cases, this infection has resulted in patient death.
- Allegations were made that these infections had been caused by non-tuberculous mycobacteria, such as *Mycobacterium chimaera*, which had been emitted by the heater-cooler.
- Because the symptoms may be slow to manifest, it is possible that many months may pass after completion of the surgical procedure before a patient presents with an endocarditis infection; this is why an association between this infection and the heater-cooler had never previously been made.
- The probability associated with this new risk has been classified as “very low.” This risk assessment is still valid and up to date, and it has been recently confirmed by independent external sources.²

May 2014 – Sorin created a task force

- Sorin has created a task force to mitigate this newly identified risk. This task force is led by Sorin QA and includes specialists from R&D, Global Marketing and Technical Service.
- Expert external consultants and accredited laboratories for water management and hygiene have been involved.

July 2014 – Sorin informed all 3T heater-cooler users

- At this stage of the investigation, the comparison of the strains found in infected patients and the strain found in the heater-cooler could not confirm that the patient infection was related to the use of the heater-cooler.
- However, the task force could confirm the presence of mycobacteria in the water circuit of devices returned from the field. This provided sufficient evidence that the level of awareness regarding the importance of keeping the water “clean” by meticulously following disinfection and maintenance procedures was potentially underestimated.
- Therefore, an “Important Information” letter³ was sent to all Sorin 3T heater-cooler users informing them about the newly identified risk and reminding them of the importance of performing the water disinfection procedures strictly according to the instructions for use (IFU). The following were provided along with the letter:
 - Mycobacteria information
 - Excerpt of the IFU about disinfection
 - Customer response form for confirmation and Sorin contact information

August 2014 – A step ahead in the investigation

- Two research groups reported results of air sampling performed in the vicinity of the heater-cooler, confirming the presence of the mycobacteria outside of the heater-cooler when switched on. This experiment was later reproduced by Sorin, lending credibility to the scenario of a patient potentially becoming infected by bacteria contained in the water circuit.
- Solutions to block or contain the emission of mycobacteria outside of the heater-cooler were initiated.

August 2014 – Minimizing potential risks of water contamination

- Additional disinfection steps were added at the end of the 3T heater-cooler manufacturing line to minimize the risk of bacterial contamination in devices released from production.

December 2014 – Confirming that the disinfection procedure is effective against mycobacteria

- The validation of the disinfection procedure was conducted in the past without considering the presence of mycobacteria, which had not been identified as a potential contaminant of the water at the time the validation was performed.
- Therefore, Sorin decided to repeat the validation with a higher standard under guidelines established in an FDA draft document (which later came into force in 2015). The Sorin validation was completed successfully in April 2015.

May 2015 – Sorin starts offering a deep disinfection service for contaminated devices

- The task force realized that existing disinfection procedures would not be sufficient to reduce the risk of bacterial contamination of a heater-cooler device if it had not been properly maintained (according to IFU) for a long period of time, thus allowing a biofilm to grow in the water circuit. This biofilm could only be removed by mechanical action.
- Considering the above result, Sorin decided to set up a deep disinfection service at our Sorin Group Deutschland facilities in Munich (to be followed by facilities in the U.S., Japan, and Australia at a later date), consisting of the following:
 - Inspection and documentation of the general system condition (pictures, samples)
 - Surface cleaning and disinfection
 - Decalcification
 - Replacing of all internal tubing
 - Cleaning of water tanks
 - Chemical disinfection with Puristeril 340
 - Hot water circulation
 - Final inspection, documentation and water sampling
 - Drying of internal water components

June 2015 – Sorin informed all 3T heater-cooler users and regulatory authorities about the risk of infection

- A Field Safety Notice⁴ was sent to all Sorin 3T heater-cooler customers on a worldwide basis to provide them with solutions to safely continue using their device if contamination with mycobacteria was discovered. The safety notice also informed them about the release of new instructions for use with stricter guidelines for cleaning and disinfection.
- All national regulatory authorities were informed about this Field Safety Action prepared in cooperation with some European regulators.
- The original 3T heater-cooler disinfection concept remained unchanged, as it was proven effective. However, the entire hygiene concept was enhanced by introducing the following modifications:
 - Filtered tap water is to be used when filling the device.
 - Instead of three different procedures (every five days; every two weeks; every three months) there are only two different procedures (every seven days; every two weeks) to make disinfection easier in daily work.
 - The option to use peracetic acid (Puristeril 340, Peresal, Minncare) instead of chloride solution (Clorox).
 - H₂O₂ in low dose for preservation.
 - All external tubing, bottles and buckets are included in the disinfection process.
 - Polyethylene tubing that meets national drinking water standards must be used.
 - Unused heater-coolers must also be disinfected biweekly.

August 2015 – Sorin provided additional information to all 3T heater-cooler users in the United States

- Sorin issued a communication⁸ to all U.S. customers to inform them that the Heater-Cooler System 3T Operating Instructions provided with the Field Safety Notice dated June 15, 2015 were intended for distribution to English speaking countries in the

European Union (EU) and Intercontinental region (IC) rather than for the United States.

- Sorin provided U.S. 3T customers a copy of the correct version of Heater-Cooler System 3T Operating Instructions.
- Sorin issued a communication⁵ with important questions and answers on this topic.
- Sorin made a quick-start instruction leaflet⁶ and a training video⁷ available on the Sorin website to explain and demonstrate each step of the disinfection as well as handling of the device and its accessories to ensure proper procedures are followed.

October 2015 – 80 devices disinfected - Further research ongoing

- So far more than 80 heater-coolers have gone through the deep disinfection service at our Sorin Group Deutschland facilities in Munich.
- Sorin will open additional deep disinfection service stations in the U.S., Japan and Australia in the coming months to better serve our customers on a global basis.
- Facilities are increasingly aware of the need for proper disinfection, and research and testing on a more robust hygiene solution is ongoing. Sorin is committed to maximize our efforts to further reduce the risk of emission in the operating theatre while reducing the workload for hospital teams responsible for keeping the device clean.

From the moment Sorin was made aware of this issue, we have been working closely with all national health authorities, who have been informed of the ongoing field safety action. Sorin continues to collaborate with heater-cooler users globally to help clinicians address this new situation and meet the demands generated by a rapidly growing level of awareness.

Thank you for your continued support and cooperation in this matter. We will continue to keep you informed about our progress in the investigation and on eventual new findings.

Sorin Group is always committed to providing the highest quality products and service to its customers, and we apologize for any inconvenience this situation may have caused for you and your teams.

Sincerely,



Thierry Dupoux
VP, Quality Assurance and Regulatory Affairs
Cardiac Surgery Business Unit

References:

- 1) "Heater-Cooler Devices_ FDA Safety Communication – Use of Devices Associated With Nontuberculous Mycobacteria Infections" – October 2015
- 2) "Infections Associated with Heater Cooler Units Used in Cardiopulmonary Bypass and ECMO" - published by Public Health England – June 2015
- 3) "IMPORTANT INFORMATION Cardiac Surgery Mycobacterium Risks" - Sorin letter July 2014
- 4) "Cardiac Surgery Mycobacterium Risks Disinfection and Cleaning of Sorin Heater Cooler devices" - Sorin Field Safety Action - June 2015
- 5) "Q&A information" – August 2015
- 6) "3T Disinfection - Quick start instruction leaflet" - August 2015
- 7) "3T Disinfection - Training video" - August 2015
- 8) "U.S. 3T FSN Update Packet" – August 2015