

LivaNova Customer Communication Update

Over the past two years, LivaNova¹ and the broader cardiac surgery community has learned a great deal about a newly-identified infection risk to open-heart surgery patients called Nontuberculous Mycobacterium (NTM). NTM are widespread in nature and are commonly found in the soil, natural water, drinking water distribution systems, and household and building plumbing, especially in recirculating hot water systems in hospitals and apartment buildings. NTM are typically not harmful, but in rare cases may cause infections in very ill patients or individuals with compromised immune systems.

NTM infections have most commonly been associated with transmission via inhalation of NTM-laden aerosols, leading to pulmonary disease in certain susceptible populations. However, recently in Europe and the US, NTM infections have been identified in patients that have previously undergone open chest cardiothoracic surgeries and were exposed to heater-cooler devices (HCDs) during surgery. The U.S. Food and Drug Administration (FDA) has stated that while it believes these NTM infections are currently uncommon and that the benefits of open chest cardiac surgery with cardiopulmonary bypass outweigh the risks in appropriately-selected patients, the NTM infections that have been reported in the US and Europe linked to prior cardiothoracic procedures have caused serious illness and in some cases have resulted in death.

As the market leader for HCDs, LivaNova is committed to patients and the clinicians who use our devices. We take seriously the rare but concerning potential risk of NTM infections and the issues raised in the FDA's recent Safety Communication. We are committed to ensuring clinician confidence in HCDs, which are critical components of cardiac surgery procedures. In this regard, we would like to provide you with an update on this important industry issue.

As noted above, HCDs have been recognized by FDA and others as serving a critical role in life-supporting and life-sustaining cardiothoracic procedures. These devices are typically located inside the operating room but outside the sterile field, and use closed, non-sterile water circuits whereby no contact with patient's blood or body fluids takes place at any time. However, analyses have shown that although the water in the HCD circuits does not come into direct contact with the patient's blood or body fluids, there is a potential for NTM-contaminated water in the HCD's water tanks to be dispersed outside of the HCD into the ambient air of the operating room through a process called aerosolization. In turn, this creates the potential for the aerosolized bacteria to ultimately come into direct contact with the patient through the open chest during the surgical procedure. FDA has stated that its review of information from HCD manufacturers shows that all HCDs currently in the market have design features that could lead to aerosol formation.

In early June 2016 FDA issued a Safety Communication citing a recently-published article by *Eurosurveillance*² describing a link between *Mycobacterium chimaera* found in contaminated heater-

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

² Haller, S., Hölle, C., Jacobshagen, A., Hamouda, O., Abu Sin, M., Monnet, D., Eckmanns, T. (2016). Contamination During Production of Heater-Cooler Units by *Mycobacterium chimaera* Potential Cause for Invasive Cardiovascular Infections: Results of an Outbreak Investigation in Germany, April 2015 to February 2016. *Eurosurveillance*, 21(17). Available at <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=22461>

cooler devices associated with patient infections and in the processing line at our production facility in Germany. We have attached a copy of the Safety Communication, which can also be found at <http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm504213.htm>. In order to help answer questions related to the Safety Communication, we have also created a brief FAQ that you will find attached to this email. This FAQ will be made available, along with other relevant information, on the 3T Heater-Cooler section of the LivaNova website at <http://www.livanova.sorin.com//3t>.

The FDA Safety Communication also noted the recent meeting of the Circulatory System Devices Panel of the Medical Devices Advisory Committee Meeting to discuss NTM infections associated with heater-cooler devices during cardiothoracic surgery. This Advisory Committee meeting took place in early June 2016, with full participation by LivaNova representatives. The Advisory Committee was asked to make recommendations on short-term and long-term mitigations, including:

- mitigating water contamination and biofilm formation in heater-cooler devices and the water circuit;
- case definition and patient and provider notifications, and
- present and future device design considerations for reducing the risk of NTM infections.

During the meeting, the FDA and the Advisory Committee reviewed the available data and sought expert scientific and clinical opinion related to HCD contamination, associated patient infections, and mitigation strategies. The FDA recently released a post-meeting summary, which provides a general overview of the discussion and general recommendations arising out of the Advisory Committee. This summary, together with all of the Advisory Committee materials, can be found on the FDA website at <http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/CirculatorySystemDevicesPanel/ucm485091.htm>

As FDA stated in its Advisory Committee summary, “[t]his public health concern is multi-faceted, involving an entire class of devices and a complex array of issues.” LivaNova will continue to engage with FDA and other stakeholders in proactively seeking appropriate methods to mitigate potential risk for NTM infections, and will continue to communicate new and updated information related to this important patient safety matter. If you have questions that are not answered within this document, the attachments or the linked information, please submit them to 3T.US@LivaNova.com.