IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MINNESOTA

DANNA BRACKENBURY, individually, and as Trustee for the Heirs and Next of Kin of Terrance Lee Brackenbury, Plaintiff, v. SORIN GROUP DEUTSCHLAND GMBH, and SORIN GROUP USA, INC., jointly and individually, Defendants.	Case No. 17-cv-4186 Jury Trial Demanded

COMPLAINT

Plaintiff Danna Brackenbury, in her own right and as Trustee for the Heirs and Next of Kin of Terrance Lee Brackenbury, through her Complaint, and pursuant to Minn. Stat. § 573.02, brings this action against Defendants Sorin Group Deutschland GmbH and Sorin Group USA, Inc. (collectively, "Sorin") hereby alleges as follows:

THE PARTIES

1. Plaintiff Danna Lynne Brackenbury is the Wife and Trustee to the Heirs and Next of Kin of Terrance Lee Brackenbury, deceased, and is a citizen of New Mexico, residing at 1674 Calle de Oriente Norte, Santa Fe, NM 87507.
2. Plaintiff, as the appointed Trustee for the Heirs and Next of Kin of Terrance Brackenbury, brings this action, in relevant part, pursuant to Minnesota's Wrongful Death statute, Minn. Stat. § 573.02 et seq. Plaintiff, as the surviving spouse of Terrance Brackenbury, brings this action, individually, for her Loss of Consortium claim.

3. Defendant Sorin Group Deutschland GbmH ("Sorin GmbH") is a foreign corporation with its headquarters in Munich, Germany. Sorin GmbH is a wholly owned subsidiary of LivaNova, PLC. Sorin GmbH designed, tested, assembled, manufactured, marketed, distributed, and/or sold the Sorin 3T Heater-Cooler Device that was used in Terrance Brackenbury's heart surgery on April 17, 2015.

4. Defendant Sorin Group, USA, Inc. ("Sorin USA") is a Delaware Corporation with its principal place of business at 14401 West 65th Way, Arvada, Colorado 80004. Sorin USA is a wholly owned subsidiary of LivaNova, PLC. Sorin USA designed, tested, assembled, manufactured, marketed, distributed, and/or sold the Sorin 3T Heater-Cooler Device that was used in Terrance Brackenbury's heart surgery on April 17, 2015. Sorin USA is a registered corporation with the Minnesota Secretary of State. Sorin USA's registered agent in Minnesota is CT Corporation System, Inc., residing at 1010 Dale St. N, St. Paul, MN 55117-5603.

JURISDICTION AND VENUE

5. Personal Jurisdiction exists over Sorin GmbH and Sorin USA (collectively, "Sorin") pursuant to Minnesota Statute § 543.19 (the "long-arm" statute) and federal due process standards because Sorin regularly conducted business in Minnesota and maintained systematic and continuous contact with Minnesota. Furthermore, Sorin designed, tested, assembled, manufactured, marketed, distributed, and/or sold the Sorin 3T Heater-Cooler Device that was used in Terrance Brackenbury's heart surgery. Upon information and belief, Sorin sold the Sorin 3T Heater-Cooler Device directly to Regions Hospital in St. Paul, Minnesota, where Mr. Brackenbury's heart surgery took place.

6. This Court has Subject Matter Jurisdiction over this action pursuant to 28 U.S.C. § 1332 because complete diversity exists between the parties and the amount in controversy exceeds $75,000.

7. Venue is proper in the District of Minnesota pursuant to 28 U.S.C. § 1391(a)(2) because a substantial part of the events or omissions giving rise to the causes of action occurred in Minnesota, and pursuant to 28 U.S.C. § 1391(c) because Defendants are subject to Personal Jurisdiction in the District of Minnesota.

FACTUAL ALLEGATIONS

8. Plaintiff incorporates by reference each and every allegation in this Complaint, as if fully set forth herein.

9. The Sorin 3T Heater-Cooler Device ("Sorin 3T") is intended to provide temperature-controlled water to heat exchanger devices (cardio-pulmonary bypass heat exchangers, cardioplegia heat exchangers, and thermal regulating blankets) to warm or cool a patient during cardio-pulmonary bypass procedures lasting six (6) hours or less. The Sorin 3T is not intended to come into contact with the patient.

10. The Sorin 3T is a Class II Medical Device that is subject to the Food and Drug Administration's ("FDA") Section 510(k) Premarket Notification process.

11. Prior to commercialization of the Sorin 3T in the United States, Sorin submitted a 510(k) Premarket Notification of intent to market the Sorin 3T with the Department of Health and Human Services. A letter from the FDA dated June 6, 2006, informed Sorin that the FDA

determined the Sorin 3T to be substantially equivalent to legally marketed predicate devices that do not require a premarket approval (PMA) application.[1]

12. Following the 510(k) approval in 2006, and at all relevant times, Sorin was in the business of designing, licensing, manufacturing, distributing, marketing, advertising, selling, and/or delivering the Sorin 3T into the stream of commerce in the United States and Minnesota, including marketing, selling, and/or delivering the Sorin 3T that was used in Mr. Brackenbury's heart surgery.

13. At all relevant times, Sorin was required to develop and test safe cleaning/disinfection protocols for the Sorin 3T, and to provide safe cleaning/disinfection instructions in the Sorin 3T's labeling and Instructions for Use ("IFU").

14. The development and testing of the cleaning/disinfection procedures conducted by Sorin was done without consideration for the presence of mycobacteria, and the instructions for cleaning/disinfecting the Sorin 3T in the IFU and elsewhere were insufficient to properly disinfect the Sorin 3T from the presence of mycobacteria.

15. Between April 11 and April 13, 2011, the FDA conducted an inspection of Sorin GmbH's manufacturing facility. Upon information and belief, this is the same facility that designed, manufactured, and/or assembled the Sorin 3T that was used in Mr. Brackenbury's heart surgery on April 17, 2015.

16. The FDA's 2011 Establishment Inspection Report found several issues related to the cleaning/disinfecting of the Sorin 3T. Specifically, the inspector found that (i) the design inputs do not include an input for the cleaning of the water tank to prevent bacterial growth;

[1] The 510(k) approval is attached as Ex A. All exhibits are incorporated as referenced herein.

(ii) the design output includes a cleaning procedure for the U.S., but requires the use of agents that are not available in the U.S.; (iii) the design verification was not performed in relation to the U.S. cleaning IFU; (iv) risk analysis does not include possible contamination from water held in the tank in relation to the patient, operating room, or operation; and (v) design changes were not adequately verified.

17. On November 18, 2016, The European Centre for Disease Prevention and Control ("ECDC") reported that cases of infection caused by Mycobacterium chimaera ("M. chimaera") in patients who had recently undergone open-heart surgery had been reported in seven European countries (France, Germany, Ireland, the Netherlands, Spain, the UK and Switzerland).[2] The ECDC reported that the outbreaks began in 2011.

18. Based upon these outbreaks in Europe, the FDA's inspection, and their own investigation and testing, Sorin knew or should have known in 2011 of the association between non-tuberculous mycobacterium ("NTM") infections and the use of the Sorin 3T when used in open-heart surgeries.

19. Upon information and belief, on or around January 2014, Sorin received notification from a hospital that at least one patient suffered an infection following an open-heart surgery in which the Sorin 3T was used. The hospital proceeded to test all Sorin 3T units, and found that all units were contaminated with bacteria.

20. On or around July 14, 2014, Sorin issued an "Important Information" letter to hospitals that had purchased the Sorin 3T.[3] The letter warned that "Some cardiac surgery patients have been infected with a slow growing *Mycobacterium chimaera*." The letter further stated that

[2] The ECDC report is attached as Ex. B.
[3] The Important Information Letter is attached as Ex. C.

"during the investigation work it has been identified that some hospitals' heater cooler devices are contaminated."

21. On or around August 6, 2014, Sorin USA filed a MAUDE adverse event report with the FDA.[4] The event description was reported as follows:

> "The 15 pts have tested positive +afb for an atypical mycobacterium infection. All infections have been surgical site infections. The investigation is still on-going. The common denominator for the cardiac surgeries is the profusion machine. The machine has been cultured and found to have the mycobacterium in the water."

22. Upon information and belief, on or around August 2014, Sorin GmbH performed its own investigation in its manufacturing facility. That investigation revealed the presence of mycobacteria on Sorin 3T units at the manufacturing facility. Upon information and belief, this is the facility that manufactured the Sorin 3T used in Mr. Brackenbury's April 17, 2015 surgery. However, the results of this investigation were not made public until nearly two years later, when the FDA issued a Safety Communication on June 1, 2016.[5]

23. On or around June 15, 2015, Sorin issued a Field Safety Notice[6] related to Mycobacterium risk and the Sorin 3T. The Field Safety Notice warned as follows:

> "Without vigilant performance of the disinfection and maintenance procedures per the Instructions for Use, organisms can multiply in a heater cooler device and potentially form biofilm. The biofilm provides an opportunity for bacteria, including Mycobacteria, to colonize within the device. Once colonized, there is a possibility that bacteria can become aerosolized when the heater cooler device is operated and serve as a source for contamination. Although water from the heater cooler device is not intended to contact the patient directly, fluid leakage from the device or aerosolization generated by a contaminated water circuit during device operation may create conditions in which organism could potentially contact the patient and subsequently contaminate the surgical site."

[4] The MAUDE report is attached as Ex. D.
[5] The June 1, 2016 Safety Communication is attached as Ex. E.
[6] The Field Safety Notice is attached as Ex. F.

24. The June 15, 2015 Field Safety Notice also included an updated IFU, which provided updated cleaning and disinfection procedures. However, these updated cleaning/disinfecting procedures were still ineffective and failed to properly clean and disinfect the Sorin 3T.

25. On or around July 15, 2015, Sorin issued a Class 2 Recall of the Sorin 3T. Sorin reported the reason for the recall as, "Potential colonization of organisms, including Mycobacteria, in Sorin Heater Cooler Devices, if proper disinfection and maintenance is not performed per Instructions for Use."[7]

26. By the time the Class 2 recall and Field Safety Notice were issued, Sorin knew, or should have known, that design and/or manufacturing defects in the Sorin 3T rendered the device prone to colonization and transmission of bacteria, including Mycobacteria, regardless of the cleaning and/or disinfection procedures used.

27. On or around August 24 to August 27, 2015, the FDA conducted a follow-up investigation at the Sorin manufacturing facility. The FDA's 2015 investigation noted that several problems continued to exist related to lack of a validated cleaning and disinfecting process for the Sorin 3T. This was the same or similar problem that the FDA identified in its 2011 inspection.

28. On or around October 15, 2015, the FDA issued a Safety Communication in regard to the Sorin 3T.[8] That Safety Communication stated that between January 2010 and August 2015, that FDA had received thirty-two (32) Medical Device Reports of patient infections associated with the Sorin 3T.

[7] The July 15, 2015 Class 2 Recall Notice is attached as Ex. G.
[8] The October 15, 2015 Safety Communication is attached as Ex. H.

29. On December 29, 2015, the FDA sent a Warning Letter to the C.E.O. of LivaNova, the parent company of Sorin GmbH and Sorin USA.[9] The Warning Letter stated that several violations of the Food, Drug, and Cosmetic Act ("FDCA") were present with respect to the Sorin 3T, including, among other things, the following:

    a. That the Sorin 3T devices are adulterated within the meaning of section 501(h) of the FDCA, 21 U.S.C. § 351(h), in that the methods used in, or the facilities or controls used for, their manufacture, packing, storage, or installation are not in conformity with the current good manufacturing practice requirements of the Quality System regulation of title 21, Code of Federal Regulations (CFR), part 820.

    b. Failure to establish and maintain procedures for the identification, documentation, validation, or where appropriate verification, review, and approval of design changes before their implementation, as required by 21 CFR 820.30(i).

    c. Failure to adequately update the cleaning and disinfection IFU after receiving complaints of patient death due to infections caused by the Sorin 3T. The updated cleaning and disinfection test does not demonstrate an adequate verification or validation of the new cleaning IFU because the acceptance criteria do not demonstrate an adequate level reduction for bacteria. Additionally, Puristeril is not available in the U.S., and therefore Sorin recommends substituting Clorox, but the test report does not demonstrate the amounts of Clorox described in the IFU are equivalent to Puristeril.

[9] The Warning Letter is attached as Ex. I.

d. Failure to validate a process, with a high degree of assurance and approved according to established procedures, where process results cannot be fully verified by subsequent inspection and test, as required by 21 CFR 820.75(a).

e. Failure to adequately develop, implement, and maintain written MDR (Medical Device Research) procedures, as required by 21 CFR 803.17.

30. On or around April 18, 2016, EuroSurveillance published an article entitled, "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" (the "EuroSurveillance article").[10]

31. The EuroSurveillance article reported the following:

> "Invasive infections with *Mycobacterium chimaera* were reported in patients with previous open chest surgery and exposure to contaminated heater-cooler units (HCUs) . . . Clinical infections occurred in five male German cases over 50 years of age (range 53–80). Cases had been exposed to HCUs from one single manufacturer during open chest surgery up to five years prior to onset of symptoms. During environmental investigations, *M. chimaera* was detected in samples from used HCUs from three different countries and samples from new HCUs as well as in the environment at the manufacturing site of one manufacturer in Germany. Our investigation suggests that at least some of the *M. chimaera* infections may have been caused by contamination of HCUs at manufacturing site."

32. Upon information and belief, the "single manufacturer" referred to by the EuroSurveillance article is Sorin, and the manufacturing site is Sorin's facility in Munchen, Germany. Upon information and belief, this is the site where the Sorin 3T used in Mr. Brackenbury's April 17, 2015 surgery was manufactured.

[10] The EuroSurveillance article is attached as Ex. J.

33. On or around June 1, 2016, the FDA issued another Safety Communication in regard to the Sorin 3T. That Safety Communication stated, "Testing conducted by [Sorin] in August 2014 found *M. chimaera* contamination on the production line and water supply at the 3T manufacturing facility. Units from this facility can be found worldwide."

34. On or around July 2016, Sorin issued at least one MAUDE adverse event report after a hospital continued to find mycobacteria, including mycobacteria avium complex and mycobacteria intracellular complex, on the Sorin 3T. The hospital had strictly followed the updated IFU cleaning/disinfecting procedure since August 2015.[11]

35. On or around October 13, 2016, the Center for Disease Control and Prevention ("CDC") issued a Health Advisory in regard to the Sorin 3T and the risk of infection after surgery.[12]

36. The CDC Health Advisory advised hospitals to notify patients who underwent open-heart surgey involving a Sorin 3T that the device was potentially contaminated, stating that information indicated the devices "were likely contaminated with the rare bacteria *Mycobacterium chimaera* during manufacturing."

37. The CDC Health Advisory went on to state the following:

> "[The] CDC in collaboration with National Jewish Health completed a whole-genome sequencing analysis and results demonstrate that M. chimaera isolates from patients with heater-cooler associated infections and from the 3T heater-cooler devices from several U.S. hospitals (in Pennsylvania and Iowa) are all highly related to each other. This evidence for likely point-source contamination of the 3T heater-cooler devices is consistent with recent reports from Europe [links omitted] that describe matching of M. chimaera sequences from environmental isolates at the device production site in Germany and isolates from patients and devices in Europe."

[11] The adverse event report is attached as Ex. K.
[12] The CDC Health Advisory is attached as Ex. L.

38. On or around October 13, 2016, the FDA issued an updated Safety Communication regarding M. chimaera infections association with the Sorin 3T.[13] The updated Safety Communication echoed the CDC's finding that results of testing done by the CDC and National Jewish Health "strongly suggest that the tested 3T devices had a common source of *M. chimaera* contamination."

39. The design and manufacturing defects in the Sorin 3T allowed bacteria, including NTM and M. chimaera, to colonize and multiply within the water and component parts of the device. Bacteria was then able to reach the surgical site and cause infection, as it did during Mr. Brackenbury's surgery, through aerosolization, fluid leakage, or by other means.

40. Sorin knew or should have known of this risk before 2011, and clearly knew of the risk by 2014, when its *own investigation* revealed that the Sorin 3T devices were contaminated with mycobacteria at the manufacturing facility. Despite knowledge of the risk to patients and others, Sorin continued to manufacture, assemble, distribute, advertise, and/or sell the Sorin 3T to hospitals in the United States, including Minnesota.

FACTS ABOUT NONTUBERCULOUS MYCOBACTERIA (NTM)

41. Plaintiff incorporates by reference each and every allegation in this Complaint, as if fully set forth herein.

42. Nontuberculous mycobacteria, or NTM, are bacteria that are typically not harmful, but can be harmful, especially in persons with weakened immune systems, or persons who have recently undergone vascular grafting, prosthetic valve surgery, or other types of invasive surgery.

[13] The October 13, 2106 Updated Safety Communication is attached as Ex. M.

43. Because NTM are slow growing, it can take months or years for symptoms to materialize after exposure.

44. The symptoms of an NTM infection are very general, including fevers, chills, nausea, and weight loss, among others. These symptoms also make an NTM infection difficult to diagnose in early stages.

45. Mycobacterium chimaera, or M. chimaera, is a sub-species of NTM. Like other NTM infections, M. chimaera may cause serious illness and/or death.

FACTS SPECIFIC TO TERRANCE BRACKENBURY

46. Plaintiff incorporates by reference each and every allegation in this Complaint, as if fully set forth herein.

47. On or around April 15, 2015, Mr. Brackenbury suffered an ST-elevated myocardial infarction (STEMI) while exercising at a gym. He was taken to Regions Hospital in St. Paul, Minnesota.

48. On or around April 17, 2015, Mr. Brackenbury underwent an open-heart procedure at Regions Hospital. The procedure included coronary artery bypass grafting, aortic valve replacement, and ascending aortic aneurysm repair.

49. The Sorin 3T was used during Mr. Brackenbury's open-heart procedure to assist in the cooling and re-warming of Mr. Brackenbury.

50. Mr. Brackenbury contracted a latent NTM infection, specifically M. chimera, from the Sorin 3T device that was used in his open-heart surgery on April 17, 2015 at Regions Hospital. Mr. Brackenbury contracted the M. chimaera infection, which ultimately led to his illness and death, because the bacteria reached the surgical site near Mr. Brackenbury's sternum.

This occurred because the bacteria from the Sorin 3T became aerosolized during his procedure, fluid leakage occurred, by other means, and/or by some combination thereof.

51. From approximately May 2015 to September 2015, Mr. Brackenbury continued to have post-operative follow-up visits. By September 2015, Mr. Brackenbury had lost about 25 lbs. from diet and exercise, was active in cycling and Tai Chi, and was generally making an excellent recovery.

52. On or around January 2016, Mr. Brackenbury began to experience fever and chills. On or about February 25, 2016, he experienced weakness in his legs and had difficulty climbing stairs.

53. On or around July 13, 2016, Mr. Brackenbury visited Fisher's Landing Family Medicine in Vancouver, Washington, with complaints of fatigue, and sudden, rapid weight loss.

54. On or around late July 2016, Mr. Brackenbury noticed a nodule (an abnormal lump) in the sternal scar area from his April 2015 open-heart surgery.

55. On or around September 1, 2016, 17ml of a thick, cloudy fluid was aspirated from Mr. Brackenbury's sternal abscess, the area near his scar from the 2015 open-heart surgery. Given the concerns for infection, he was admitted to Oregon Health and Science University (OHSU) later that day.

56. Between around September 1 and September 6, 2016, OHSU performed a series of tests, including imaging studies of the chest and abdomen, labs and cultures to identify the source and type of infection, and Mr. Brackenbury was given antibiotics to treat suspected organisms, blood product transfusions, and other treatment methods. However, nothing was able to control the infection.

57. On or around September 7, 2016, Mr. Brackenbury underwent a redo sternotomy and drainage of multiple abscesses. Cultures taken during this procedure tested positive for acid fast bacillus. It was at this point that mycobacterium, possibly M. chimaera, was suspected as the likely cause of the infection. Samples were also sent to the University of Washington for PCR studies.

58. On or around September 12, 2016, the University of Washington Medical Center Lab confirmed the presence of mycobacterium intracellulare or M. chimaera[14] in the samples from the sternal tissue.

59. Mr. Brackenbury's treating physicians at OHSU associated his M. chimaera infection with his April 17, 2015 open-heart surgery.

60. Despite a valiant effort by OHSU to halt the infection, Mr. Brackenbury's condition worsened, and on September 14, 2016, his level of care was reduced to provide for comfort alone. He died later that day at the age of 67.

61. Mr. Brackenbury's immediate cause of death was listed as multisystem organ failure, caused by septic shock as a consequence of disseminated mycobacterium infection.

62. Genetic sequencing later confirmed that Mr. Brackenbury had been suffering from an M. chimaera infection.

COUNT I

Strict Liability – Design Defect
(On Behalf of the Heirs and Next of Kin of Terrance Brackenbury)

63. Plaintiff incorporates by reference each and every allegation in this Complaint, as if fully set forth herein.

[14] The method of testing used did not distinguish between these two organism types.

64. At all relevant times, Sorin was engaged in the design, development, testing, manufacture, assembly, promotion, marketing, and/or sale of the Sorin 3T that was used in Mr. Brackenbury's April 17, 2015 open-heart surgery.

65. The Sorin 3T was defective at the time that it was designed, manufactured, assembled, and sold. The Sorin 3T was defective in that its design prevented it from being properly and consistently cleaned and disinfected based on the accompanying IFU and other labels, instructions, or cleaning procedures, thus rendering the Sorin 3T unsafe for use by Regions Hospital, and unsafe for use in Mr. Brackenbury's open-heart surgery on April 17, 2015.

66. The Sorin 3T used by Regions Hospital in the surgery of Mr. Brackenbury on April 17, 2015, was expected to reach, and did reach, Regions Hospital and Mr. Brackenbury, the intended consumer and ultimate consumer, without substantial change to the condition in which it was sold by Sorin.

67. At the time the Sorin 3T left the possession of Sorin, the Sorin 3T was defective, and its condition made it unreasonably dangerous for Mr. Brackenbury and others who may have been exposed to the device at Regions Hospital. The Sorin 3T was defective because its design allowed bacteria, including mycobacteria, to collect and multiply and to form biofilm in the device. Said bacteria could subsequently come into contact with vulnerable patients and others in the operating room, or to infect other areas of the operating room, through aerosolization, fluid leakage, or other means.

68. Sorin intended for the Sorin 3T to be used in heart surgeries (among others) at Regions Hospital, like the one Mr. Brackenbury had on April 17, 2015. Sorin knew or should have known that the Sorin 3T would be used by patients like Mr. Brackenbury at Regions Hospital.

69. The Sorin 3T was used by Regions Hospital for Mr. Brackenbury's surgery in the manner in which it was intended, thus it was reasonably foreseeable that the Sorin 3T would be used in Mr. Brackenbury's surgery.

70. At all relevant times, Mr. Brackenbury could not have discovered the design defects associated with the Sorin 3T through the exercise of due diligence, nor could he have been expected to perceive the danger posed by the Sorin 3T. Thus, the dangerous condition of the Sorin 3T was unknowable to Mr. Brackenbury.

71. The Sorin 3T, as designed by Sorin, transmitted bacteria, including M. chimaera, directly to patients undergoing invasive surgery, including Mr. Brackenbury, through aerosolization, fluid leakage, or by other means.

72. The foreseeable risks of transmitting bacteria to patients undergoing invasive surgery, including Mr. Brackenbury, far outweighs any utility of using the Sorin 3T. The foreseeable risks also far outweigh any cost of designing, manufacturing, and producing an alternative design of the Sorin 3T that is not defective.

73. Mr. Brackenbury had a reasonable expectation that the Sorin 3T would not be unreasonably dangerous and defective, and that the device would not cause him to contract the M. chimaera bacteria that would ultimately take his life.

74. The use of the Sorin 3T during Mr. Brackenbury's open-heart surgery on April 17, 2015, was the cause-in-fact of his injuries, specifically, his contraction of M. chimaera, and his subsequent disability and death.

75. As a direct and proximate result of using the Sorin 3T system during his open-heart surgery on April 17, 2015, specifically the defective design of the device, Mr. Brackenbury suffered catastrophic injury, disability, and death.

76. As a result of the foregoing, Plaintiff and the Heirs and Next of Kin of Terrance Brackenbury have incurred expenses for the funeral of the decedent and have sustained pecuniary loss within the meaning of Minn. Stat. § 573.02 and were otherwise damaged in an amount not yet determined but for which Minnesota law provides a remedy.

COUNT II

Strict Liability – Manufacturing Defect
(On Behalf of the Heirs and Next of Kin of Terrance Brackenbury)

77. Plaintiff incorporates by reference each and every allegation in this Complaint, as if fully set forth herein.

78. At all relevant times, Sorin was engaged in the design, development, testing, manufacture, assembly, promotion, marketing, and/or sale of the Sorin 3T that was used in Mr. Brackenbury's April 17, 2015 open-heart surgery.

79. The Sorin 3T was defective at the time that it was designed, manufactured, assembled, and sold. The Sorin 3T was defective in that its design and manufacture prevented it from being properly and consistently cleaned and disinfected based on the accompanying IFU and other labels, instructions, or cleaning procedures, thus rendering the Sorin 3T unsafe for use by Regions Hospital, and unsafe for use in Mr. Brackenbury's open-heart surgery on April 17, 2015.

80. The Sorin 3T's was further defective in its manufacture, in that the device was exposed to the M. chimaera bacteria at the time that the device was manufactured. This occurred because M. chimaera was present at Sorin's manufacturing facility where the Sorin 3T, including the Sorin 3T used in Mr. Brackenbury's surgery, was designed, manufactured, and/or assembled.

81. The Sorin 3T used by Regions Hospital in the surgery of Mr. Brackenbury on April 17, 2015, was expected to reach, and did reach, Regions Hospital and Mr. Brackenbury, the intended consumer and ultimate consumer, without substantial change to the condition in which it was sold by Sorin.

82. At the time the Sorin 3T left the possession of Sorin, the Sorin 3T was defective, and its condition made it unreasonably dangerous for Mr. Brackenbury and others who may have been exposed to the device at Regions Hospital. The Sorin 3T was defective because its design and manufacture allowed bacteria, including mycobacteria, to collect and multiply and to form biofilm in the device. In fact, the M. chimaera bacteria was present on the Sorin 3T at the time it left Sorin's manufacturing facility. Said bacteria could subsequently come into contact with vulnerable patients and others in the operating room, or to infect other areas of the operating room, through aerosolization, fluid leakage, or other means.

83. Sorin intended for the Sorin 3T to be used in heart surgeries (among others) at Regions Hospital, like the one Mr. Brackenbury had on April 17, 2015. Sorin knew or should have known that the Sorin 3T would be used by patients like Mr. Brackenbury at Regions Hospital.

84. The Sorin 3T was used by Regions Hospital for Mr. Brackenbury's surgery in the manner in which it was intended, thus it was reasonably foreseeable that the Sorin 3T would be used in Mr. Brackenbury's surgery.

85. At all relevant times, Mr. Brackenbury could not have discovered the manufacturing defects associated with the Sorin 3T through the exercise of due diligence, nor could he have been expected to perceive the danger posed by the Sorin 3T. Thus, the dangerous condition of the Sorin 3T was unknowable to Mr. Brackenbury.

86. The Sorin 3T, as designed by Sorin, transmitted bacteria, including M. chimaera, directly to patients undergoing invasive surgery, including Mr. Brackenbury, through aerosolization, fluid leakage, or by other means.

87. The foreseeable risks of transmitting bacteria to patients undergoing invasive surgery, including Mr. Brackenbury, far outweighs any utility of using the Sorin 3T.

88. Sorin failed to prevent the Sorin 3T from being manufactured, assembled, and/or prepared to be distributed in a manner that would have prevented the device from being contaminated while on the production line or elsewhere while in Sorin's possession or control.

89. Sorin manufactured, assembled, and/or sold the Sorin 3T with NTM including M. chimaera, present in and/or on the device. The contamination occurred on the production line or elsewhere while in Sorin's possession or control.

90. Sorin's failure to ensure proper sanitation in the workplace, failure to ensure proper workmanship, failure to ensure adequate testing of component parts, and/or failure to ensure adequate labeling for the Sorin 3T caused the Sorin 3T to be manufactured in a manner that made the device defective and unreasonably dangerous.

91. Mr. Brackenbury had a reasonable expectation that the Sorin 3T would not be unreasonably dangerous and defective, and that the device would not cause him to contract the M. chimaera bacteria that would ultimately take his life.

92. The use of the Sorin 3T during Mr. Brackenbury's open-heart surgery on April 17, 2015, was the cause-in-fact of his injuries, specifically, his contraction of M. chimaera, and his subsequent disability and death.

93. As a direct and proximate result of using the Sorin 3T system during his open-heart surgery on April 17, 2015, specifically the defective manufacture the device, Mr. Brackenbury suffered catastrophic injury, disability, and death.

94. As a result of the foregoing, Plaintiff and the Heirs and Next of Kin of Terrance Brackenbury have incurred expenses for the funeral of the decedent and have sustained pecuniary loss within the meaning of Minn. Stat. § 573.02 and were otherwise damaged in an amount not yet determined but for which Minnesota law provides a remedy.

COUNT III

Strict Liability – Failure to Warn
(On Behalf of the Heirs and Next of Kin of Terrance Brackenbury)

95. Plaintiff incorporates by reference each and every allegation in this Complaint, as if fully set forth herein.

96. At all relevant times, Sorin was engaged in the design, development, testing, manufacture, assembly, promotion, marketing, and/or sale of the Sorin 3T that was used in Mr. Brackenbury's April 17, 2015 open-heart surgery.

97. The Sorin 3T was defective at the time that it was designed, manufactured, assembled, and sold. The Sorin 3T was defective in that its design and manufacture prevented it from being properly and consistently cleaned and disinfected based on the accompanying IFU and other labels, instructions, or cleaning procedures, thus rendering the Sorin 3T unsafe for use by Regions Hospital, and unsafe for use in Mr. Brackenbury's open-heart surgery on April 17, 2015.

98. The Sorin 3T was further defective and unreasonably dangerous in that the "IFU" and other labels and materials failed to adequately warn hospital staff, patients, and others, about the

Sorin 3T's serious risk of causing infection from aerosolization and/or fluid leakage from the device, which can lead to serious infections and death.

99. At all relevant times, Sorin was aware of the Sorin 3T's defects which caused the unreasonably dangerous condition.

100. The Sorin 3T was in a defective condition at the time it left Sorin.

101. Sorin failed to timely and adequately warn hospitals/healthcare providers and patients of the serious risks associated with the Sorin 3T, including, but not limited to:

    a. That the Sorin 3T was contaminated with NTM, specifically M. chimaera, at the time the device was manufactured;

    b. That the Sorin 3T could harbor and grow bacteria, including M. chimaera;

    c. That the bacteria, including M. chimaera, can reach the surgical site during an operation through aerosolization, fluid leakage, and/or other methods.

102. Further, Sorin failed to adequately and timely provide cleaning and disinfecting procedure that ensured that the Sorin 3T would not continue to be contaminated with bacteria, including M. chimaera.

103. Mr. Brackenbury had a reasonable expectation that the Sorin 3T would not be unreasonably dangerous and defective, that Sorin provided all proper warnings and IFU regarding the Sorin 3T, and that the device would not cause him to contract the M. chimaera bacteria that would ultimately take his life.

104. If Plaintiff or Mr. Brackenbury had been made aware of the significant risks of NTM and M. chimaera infection associated with the use of the Sorin 3T, Mr. Brackenbury would not have consented to use of the Sorin 3T during his April 17, 2015 surgery.

105. The use of the Sorin 3T during Mr. Brackenbury's open-heart surgery on April 17, 2015, was the cause-in-fact of his injuries, specifically, his contraction of M. chimaera, and his subsequent disability and death.

106. As a direct and proximate result of using the Sorin 3T system during his open-heart surgery on April 17, 2015, and as a result of Sorin's failure to warn, Mr. Brackenbury suffered catastrophic injury, disability, and death.

107. As a direct and proximate cause of Sorin's failure to warn Regions Hospital, Plaintiff, Mr. Brackenbury, the FDA, and the public about the significant risk of NTM and M. chimaera infection from use of the Sorin 3T in surgery, Mr. Brackenbury suffered catastrophic injury, disability, and death.

108. As a result of the foregoing, Plaintiff and the Heirs and Next of Kin of Terrance Brackenbury have incurred expenses for the funeral of the decedent and have sustained pecuniary loss within the meaning of Minn. Stat. § 573.02 and were otherwise damaged in an amount not yet determined but for which Minnesota law provides a remedy.

COUNT IV

Negligence
(On Behalf of the Heirs and Next of Kin of Terrance Brackenbury)

109. Plaintiff incorporates by reference each and every allegation in this Complaint, as if fully set forth herein.

110. Sorin owed a duty of reasonable care to the public and all foreseeable users of the Sorin 3T, including patients, when it designed, tested, assembled, manufactured, marketed, distributed, and sold the Sorin 3T into the stream of commerce. This duty of reasonable care required Sorin to assure that the product was in full compliance with FDA and other

regulations, and was not defective or unreasonably dangerous for its intended purpose and other foreseeable uses.

111. Sorin breached this duty of care by designing, testing, assembling, manufacturing, marketing, distributing, and selling the Sorin 3T in a manner that made the device defective and unreasonably dangerous for its intended and foreseeable use. This defect stems from the Sorin 3T's propensity to permit the colonization and growth of bacteria, including NTM and M. chimaera, and the ability of said bacteria to reach the surgical site through aerosolization, fluid leakage, or other means.

112. Sorin further breached this duty by allowing the Sorin 3T devices, including the device used in Mr. Brackenbury's open-heart surgery, to become contaminated with NTM and M. chimaera while still in Sorin's possession and control, and then sold to the end user without being disinfected.

113. Sorin owed Plaintiff and Mr. Brackenbury a duty of reasonable care to discover these defects and to timely warn the FDA, Regions Hospital, and Mr. Brackenbury about these defects.

114. Sorin failed to timely warn the FDA, Regions Hospital, and Mr. Brackenbury about these defects, thereby breaching its duty of care.

115. Sorin owed a duty to Plaintiff, Mr. Brackenbury, all foreseeable users, and the general public to develop, test, and produce a cleaning and disinfecting procedure to be included in the IFU that adequately eliminated the presence of NTM and M. chimaera from the Sorin 3T.

116. Sorin failed to develop, test, and produce a cleaning and disinfecting procedure that adequately eliminated the presence of NTM and M. chimaera from the Sorin 3T, thereby breaching its duty of care.

117. Sorin owed a duty to Plaintiff, Mr. Brackenbury, all foreseeable users, and the general public to issue a timely recall of all Sorin 3T units in use throughout the United States and abroad when Sorin became aware that the Sorin 3T unites had become contaminated at Sorin's manufacturing facility.

118. Sorin breached this duty by failing to timely recall all Sorin 3T devices, despite Sorin's knowledge that the devices had been exposed to the M. chimaera bacteria and were possibly contaminated.

119. As a direct and proximate cause of Sorin's breach of duty, Mr. Brackenbury became infected with M. chimaera as a result of bacteria from the Sorin 3T reaching the surgical site—at his open chest—on April 17, 2015.

120. As a direct and proximate cause of Sorin's breach of duty, Mr. Brackenbury became seriously ill with infection, and ultimately died as a result of the M. chimera infection.

121. As a result of the foregoing, Plaintiff and the Heirs and Next of Kin of Terrance Brackenbury have incurred expenses for the funeral of the decedent and have sustained pecuniary loss within the meaning of Minn. Stat. § 573.02 and were otherwise damaged in an amount not yet determined but for which Minnesota law provides a remedy.

COUNT V

Loss of Consortium
(On Behalf of Danna Brackenbury)

122. Plaintiff incorporates by reference each and every allegation in this Complaint, as if fully set forth herein.

123. Plaintiff Danna Brackenbury was entitled to the care, comfort, companionship, services, and consortium of her husband, Terrance Brackenbury.

124. As a direct and proximate result of the negligence, carelessness, and willful and wanton conduct by Sorin as outlined herein, Mr. Brackenbury contracted an M. chimaera infection, fell severely ill, and lost his life.

125. As a result of the injuries and wrongful death of Terrance Brackenbury, Plaintiff was, and will continue to be, deprived of care, comfort, companionship, services, and consortium of her Husband.

126. As a result of the foregoing, Plaintiff incurred damages related to the loss of Terrance Brackenbury's services and companionship that she would have received in the usual course of married life, and other damages reasonable under the circumstances for which Minnesota law provides a remedy.

ACTUAL DAMAGES

127. Plaintiff incorporates by reference each and every allegation in this Complaint, as if fully set forth herein.

128. As a direct and proximate result of the acts, omissions, and violations of Defendants as alleged herein, Plaintiff has suffered injuries and damages. Plaintiff seeks compensation from Defendants for injuries including, but not limited to:

    a. Pecuniary losses resulting from the death of Mr. Brackenbury;

    b. Loss of consortium damages incurred by Mrs. Brackenbury;

    c. Medical bills and expenses, including funeral expenses;

    d. Any and all such further relief to which Plaintiff may be entitled under the law.

PRAYER FOR RELIEF

129. Plaintiff incorporates by reference each and every allegation in this Complaint, as if fully set forth herein.

130. Plaintiff, Danna Brackenbury, in her own right and as Trustee on Behalf of the Heirs and Kin of Terrance Brackenbury, requests the Court to enter judgment against the Defendants, jointly and individually, for a reasonable amount greater than $75,000, together with interests, costs, and disbursements incurred herein.

PLAINTIFF HEREBY DEMANDS A TRIAL BY JURY

Dated: September 8, 2017

[redacted]

Attorneys for Plaintiff

JS 44 (Rev. 06/17)

CIVIL COVER SHEET

The JS 44 civil cover sheet and the information contained herein neither replace nor supplement the filing and service of pleadings or other papers as required by law, except as provided by local rules of court. This form, approved by the Judicial Conference of the United States in September 1974, is required for the use of the Clerk of Court for the purpose of initiating the civil docket sheet. *(SEE INSTRUCTIONS ON NEXT PAGE OF THIS FORM.)*

I. (a) PLAINTIFFS

Danna Brackenbury, individually, and as Trustee for the Heirs and Next of Kin of Terrance Lee Brackenbury

(b) County of Residence of First Listed Plaintiff Santa Fe County, NM
(EXCEPT IN U.S. PLAINTIFF CASES)

(c) Attorneys *(Firm Name, Address, and Telephone Number)*

[redacted]

DEFENDANTS

Sorin Group Deutschland GMBH, and Sorin Group USA, Inc.

County of Residence of First Listed Defendant
(IN U.S. PLAINTIFF CASES ONLY)

NOTE: IN LAND CONDEMNATION CASES, USE THE LOCATION OF THE TRACT OF LAND INVOLVED.

Attorneys *(If Known)*

II. BASIS OF JURISDICTION *(Place an "X" in One Box Only)*

- ❒ 1 U.S. Government Plaintiff
- ❒ 3 Federal Question *(U.S. Government Not a Party)*
- ❒ 2 U.S. Government Defendant
- ☒ 4 Diversity *(Indicate Citizenship of Parties in Item III)*

III. CITIZENSHIP OF PRINCIPAL PARTIES *(Place an "X" in One Box for Plaintiff and One Box for Defendant)*

(For Diversity Cases Only)

	PTF	DEF		PTF	DEF
Citizen of This State	❒ 1	❒ 1	Incorporated *or* Principal Place of Business In This State	❒ 4	❒ 4
Citizen of Another State	☒ 2	❒ 2	Incorporated *and* Principal Place of Business In Another State	❒ 5	☒ 5
Citizen or Subject of a Foreign Country	❒ 3	❒ 3	Foreign Nation	❒ 6	❒ 6

IV. NATURE OF SUIT *(Place an "X" in One Box Only)*

Click here for: Nature of Suit Code Descriptions.

CONTRACT
- ❒ 110 Insurance
- ❒ 120 Marine
- ❒ 130 Miller Act
- ❒ 140 Negotiable Instrument
- ❒ 150 Recovery of Overpayment & Enforcement of Judgment
- ❒ 151 Medicare Act
- ❒ 152 Recovery of Defaulted Student Loans (Excludes Veterans)
- ❒ 153 Recovery of Overpayment of Veteran's Benefits
- ❒ 160 Stockholders' Suits
- ❒ 190 Other Contract
- ❒ 195 Contract Product Liability
- ❒ 196 Franchise

TORTS

PERSONAL INJURY
- ❒ 310 Airplane
- ❒ 315 Airplane Product Liability
- ❒ 320 Assault, Libel & Slander
- ❒ 330 Federal Employers' Liability
- ❒ 340 Marine
- ❒ 345 Marine Product Liability
- ❒ 350 Motor Vehicle
- ❒ 355 Motor Vehicle Product Liability
- ❒ 360 Other Personal Injury
- ❒ 362 Personal Injury - Medical Malpractice

PERSONAL INJURY
- ☒ 365 Personal Injury - Product Liability
- ❒ 367 Health Care/ Pharmaceutical Personal Injury Product Liability
- ❒ 368 Asbestos Personal Injury Product Liability

PERSONAL PROPERTY
- ❒ 370 Other Fraud
- ❒ 371 Truth in Lending
- ❒ 380 Other Personal Property Damage
- ❒ 385 Property Damage Product Liability

FORFEITURE/PENALTY
- ❒ 625 Drug Related Seizure of Property 21 USC 881
- ❒ 690 Other

BANKRUPTCY
- ❒ 422 Appeal 28 USC 158
- ❒ 423 Withdrawal 28 USC 157

PROPERTY RIGHTS
- ❒ 820 Copyrights
- ❒ 830 Patent
- ❒ 835 Patent - Abbreviated New Drug Application
- ❒ 840 Trademark

OTHER STATUTES
- ❒ 375 False Claims Act
- ❒ 376 Qui Tam (31 USC 3729(a))
- ❒ 400 State Reapportionment
- ❒ 410 Antitrust
- ❒ 430 Banks and Banking
- ❒ 450 Commerce
- ❒ 460 Deportation
- ❒ 470 Racketeer Influenced and Corrupt Organizations
- ❒ 480 Consumer Credit
- ❒ 490 Cable/Sat TV
- ❒ 850 Securities/Commodities/ Exchange
- ❒ 890 Other Statutory Actions
- ❒ 891 Agricultural Acts
- ❒ 893 Environmental Matters
- ❒ 895 Freedom of Information Act
- ❒ 896 Arbitration
- ❒ 899 Administrative Procedure Act/Review or Appeal of Agency Decision
- ❒ 950 Constitutionality of State Statutes

REAL PROPERTY
- ❒ 210 Land Condemnation
- ❒ 220 Foreclosure
- ❒ 230 Rent Lease & Ejectment
- ❒ 240 Torts to Land
- ❒ 245 Tort Product Liability
- ❒ 290 All Other Real Property

CIVIL RIGHTS
- ❒ 440 Other Civil Rights
- ❒ 441 Voting
- ❒ 442 Employment
- ❒ 443 Housing/ Accommodations
- ❒ 445 Amer. w/Disabilities - Employment
- ❒ 446 Amer. w/Disabilities - Other
- ❒ 448 Education

PRISONER PETITIONS

Habeas Corpus:
- ❒ 463 Alien Detainee
- ❒ 510 Motions to Vacate Sentence
- ❒ 530 General
- ❒ 535 Death Penalty

Other:
- ❒ 540 Mandamus & Other
- ❒ 550 Civil Rights
- ❒ 555 Prison Condition
- ❒ 560 Civil Detainee - Conditions of Confinement

LABOR
- ❒ 710 Fair Labor Standards Act
- ❒ 720 Labor/Management Relations
- ❒ 740 Railway Labor Act
- ❒ 751 Family and Medical Leave Act
- ❒ 790 Other Labor Litigation
- ❒ 791 Employee Retirement Income Security Act

IMMIGRATION
- ❒ 462 Naturalization Application
- ❒ 465 Other Immigration Actions

SOCIAL SECURITY
- ❒ 861 HIA (1395ff)
- ❒ 862 Black Lung (923)
- ❒ 863 DIWC/DIWW (405(g))
- ❒ 864 SSID Title XVI
- ❒ 865 RSI (405(g))

FEDERAL TAX SUITS
- ❒ 870 Taxes (U.S. Plaintiff or Defendant)
- ❒ 871 IRS—Third Party 26 USC 7609

V. ORIGIN *(Place an "X" in One Box Only)*

☒ 1 Original Proceeding ❒ 2 Removed from State Court ❒ 3 Remanded from Appellate Court ❒ 4 Reinstated or Reopened ❒ 5 Transferred from Another District *(specify)* ❒ 6 Multidistrict Litigation - Transfer ❒ 8 Multidistrict Litigation - Direct File

VI. CAUSE OF ACTION

Cite the U.S. Civil Statute under which you are filing ***(Do not cite jurisdictional statutes unless diversity)***:
28 U.S.C. § 1332, Diversity

Brief description of cause:
Wrongful Death, Products Liability

VII. REQUESTED IN COMPLAINT:

❒ CHECK IF THIS IS A **CLASS ACTION** UNDER RULE 23, F.R.Cv.P.

DEMAND $

CHECK YES only if demanded in complaint:

JURY DEMAND: ☒ Yes ❒ No

VIII. RELATED CASE(S) IF ANY

(See instructions):

JUDGE _____ DOCKET NUMBER _____

DATE
09/08/2017

SIGNATURE OF ATTORNEY OF RECORD
/s/ [redacted]

FOR OFFICE USE ONLY

RECEIPT # _____ AMOUNT _____ APPLYING IFP _____ JUDGE _____ MAG. JUDGE _____

INSTRUCTIONS FOR ATTORNEYS COMPLETING CIVIL COVER SHEET FORM JS 44

Authority For Civil Cover Sheet

The JS 44 civil cover sheet and the information contained herein neither replaces nor supplements the filings and service of pleading or other papers as required by law, except as provided by local rules of court. This form, approved by the Judicial Conference of the United States in September 1974, is required for the use of the Clerk of Court for the purpose of initiating the civil docket sheet. Consequently, a civil cover sheet is submitted to the Clerk of Court for each civil complaint filed. The attorney filing a case should complete the form as follows:

I.(a) **Plaintiffs-Defendants.** Enter names (last, first, middle initial) of plaintiff and defendant. If the plaintiff or defendant is a government agency, use only the full name or standard abbreviations. If the plaintiff or defendant is an official within a government agency, identify first the agency and then the official, giving both name and title.

(b) **County of Residence.** For each civil case filed, except U.S. plaintiff cases, enter the name of the county where the first listed plaintiff resides at the time of filing. In U.S. plaintiff cases, enter the name of the county in which the first listed defendant resides at the time of filing. (NOTE: In land condemnation cases, the county of residence of the "defendant" is the location of the tract of land involved.)

(c) **Attorneys.** Enter the firm name, address, telephone number, and attorney of record. If there are several attorneys, list them on an attachment, noting in this section "(see attachment)".

II. **Jurisdiction.** The basis of jurisdiction is set forth under Rule 8(a), F.R.Cv.P., which requires that jurisdictions be shown in pleadings. Place an "X" in one of the boxes. If there is more than one basis of jurisdiction, precedence is given in the order shown below.
United States plaintiff. (1) Jurisdiction based on 28 U.S.C. 1345 and 1348. Suits by agencies and officers of the United States are included here.
United States defendant. (2) When the plaintiff is suing the United States, its officers or agencies, place an "X" in this box.
Federal question. (3) This refers to suits under 28 U.S.C. 1331, where jurisdiction arises under the Constitution of the United States, an amendment to the Constitution, an act of Congress or a treaty of the United States. In cases where the U.S. is a party, the U.S. plaintiff or defendant code takes precedence, and box 1 or 2 should be marked.
Diversity of citizenship. (4) This refers to suits under 28 U.S.C. 1332, where parties are citizens of different states. When Box 4 is checked, the citizenship of the different parties must be checked. (See Section III below**; NOTE: federal question actions take precedence over diversity cases.**)

III. **Residence (citizenship) of Principal Parties.** This section of the JS 44 is to be completed if diversity of citizenship was indicated above. Mark this section for each principal party.

IV. **Nature of Suit.** Place an "X" in the appropriate box. If there are multiple nature of suit codes associated with the case, pick the nature of suit code that is most applicable. Click here for: Nature of Suit Code Descriptions.

V. **Origin.** Place an "X" in one of the seven boxes.
Original Proceedings. (1) Cases which originate in the United States district courts.
Removed from State Court. (2) Proceedings initiated in state courts may be removed to the district courts under Title 28 U.S.C., Section 1441. When the petition for removal is granted, check this box.
Remanded from Appellate Court. (3) Check this box for cases remanded to the district court for further action. Use the date of remand as the filing date.
Reinstated or Reopened. (4) Check this box for cases reinstated or reopened in the district court. Use the reopening date as the filing date.
Transferred from Another District. (5) For cases transferred under Title 28 U.S.C. Section 1404(a). Do not use this for within district transfers or multidistrict litigation transfers.
Multidistrict Litigation – Transfer. (6) Check this box when a multidistrict case is transferred into the district under authority of Title 28 U.S.C. Section 1407.
Multidistrict Litigation – Direct File. (8) Check this box when a multidistrict case is filed in the same district as the Master MDL docket.
PLEASE NOTE THAT THERE IS NOT AN ORIGIN CODE 7. Origin Code 7 was used for historical records and is no longer relevant due to changes in statue.

VI. **Cause of Action.** Report the civil statute directly related to the cause of action and give a brief description of the cause. **Do not cite jurisdictional statutes unless diversity.** Example: U.S. Civil Statute: 47 USC 553 Brief Description: Unauthorized reception of cable service

VII. **Requested in Complaint.** Class Action. Place an "X" in this box if you are filing a class action under Rule 23, F.R.Cv.P.
Demand. In this space enter the actual dollar amount being demanded or indicate other demand, such as a preliminary injunction.
Jury Demand. Check the appropriate box to indicate whether or not a jury is being demanded.

VIII. **Related Cases.** This section of the JS 44 is used to reference related pending cases, if any. If there are related pending cases, insert the docket numbers and the corresponding judge names for such cases.

Date and Attorney Signature. Date and sign the civil cover sheet.

EXHIBIT A
510(k) Approval

JUN - 6 2006

K052601

Traditional 510(k) Premarket Notification
510(k) Summary
Sorin Group Deutschland GmbH, Stöckert Heater-Cooler System 3T

1. SUBMITTER/HOLDER

Sorin Group Deutschland GmbH
Lindberghstrasse 25
80939 Munich
Germany

Contact: Helmut Höfl, Director, Quality Assurance and Regulatory Affairs
Telephone: 011 49 89 323 010

Date Prepared: September 19, 2005

2. DEVICE NAME

Proprietary Name: Stöckert Heater-Cooler System 3T
Common/Usual Name: Heater-Cooler
Classification Name: Cardiopulmonary bypass temperature controller

3. PREDICATE DEVICE

- Cincinnati Subzero Hemotherm (CSZ Hemotherm) (K811742)
- Alpha Omega, Inc. Dual^2 Cooler-Heater (K001520)
- Jostra AB Heater-Cooler Unit 30 (K031544)

4. DEVICE DESCRIPTION

The Sorin Group Deutschland GmbH Stöckert Heater-Cooler System 3T consists of standard and optional components. The standard components comprise the heater-cooler base unit, water connectors, CAN-connecting cable for the S3 System, potential equalization cable, and Operating Instructions. Patient blankets used with the System are already legally marketed in the United States.

5. INTENDED USE

The Stöckert Heater-Cooler System 3T is intended to provide temperature-controlled water to heat exchanger devices (cardiopulmonary bypass heat exchangers, cardioplegia heat exchangers, and thermal regulating blankets) to warm or cool a patient during cardiopulmonary bypass procedures lasting six (6) hours or less.

6. TECHNOLOGICAL CHARACTERISTICS AND SUBSTANTIAL EQUIVALENCE

Sorin Group Deutschland GmbH bases the claim of substantial equivalence of the Stöckert Heater-Cooler System 3T to the cited predicate devices based on equivalence in intended use, fundamental technological and operational characteristics. Testing submitted in this premarket notification demonstrates that the Stöckert Heater-Cooler System 3T complies with specifications, meets user requirements, and the differences between the proposed device and cited predicate devices do not raise new issues of safety or effectiveness.

EX. A

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

JUN - 6 2006

Sorin Group Deutschland GmbH
c/o Ms. Rosina Robinson
Principal Consultant, Regulatory Services
49 Plain Street
North Attleboro, MA 02760

Re: K052601
Stockert Heater-Cooler System 3T
Regulation Number: 21 CFR 870.4250
Regulation Name: Cardiopulmonary Bypass Temperature Controller
Regulatory Class: Class II
Product Code: DWC
Dated: May 15, 2006
Received: May 16, 2006

Dear Ms. Robinson:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.
This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Office of Compliance at (240) 276-0120. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (240) 276-3150 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Bram D. Zuckerman, M.D.
Director
Division of Cardiovascular Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

Indications for Use

510(k) Number: K052601

Device Name: Stöckert Heater-Cooler System 3T

Indications for Use:

The Stöckert Heater-Cooler System 3T is used with a Stöckert S3 heart-lung machine and/or any other heart lung machine featuring a separate temperature control for extracorporeal perfusion of durations of up to 6 hours.

Prescription Use ___X___ (Part 21 CFR 801 Subpart D) AND/OR Over-The-Counter Use _____ (21 CFR 807 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Donna R. Vachney

(Division Sign-Off)
Division of **Cardiovascular Devices**

510(k) Number K052601

EX. A

EXHIBIT B
The ECDC Report

RAPID RISK ASSESSMENT

Invasive cardiovascular infection by *Mycobacterium chimaera* associated with the 3T heater-cooler system used during open-heart surgery

18 November 2016

Conclusions and options for response

Fifty-two cases of invasive cardiovascular infection caused by *Mycobacterium chimaera* have been detected in patients who had previously undergone open-heart surgery in seven countries in Europe (France, Germany, Ireland, the Netherlands, Spain, the UK and Switzerland) since 2011. Cases have also been reported in the US, Canada, Australia and Hong-Kong Special Administrative Region.

Isolation of *M. chimaera* in heater-cooler units (HCUs) and in air samples suggests aerosolisation of water from the HCUs in the operating room as the most likely source of infection. Contamination of the 3T heater-cooler system at the manufacturing site in Germany, has been identified as the most plausible source, which explains most but not all of invasive *M. chimaera* infections linked to this device. Contamination during use at the hospital as well as involvement of other heater-cooler system models are also possible.

Relocation of HCUs to outside of the operating room, or other ways of strict separation of the HCU from the air volume of the operating room appear to be the safest measure. However, this solution may not be feasible in every centre. In such cases, if maintaining the HCU in the operating room is considered the only option, it should be placed at maximum distance from the operating table, the vent exhaust directed and channelled away from the patient and, if possible, close to the room air suction exhaust. However, this option may not be sufficient to eliminate the risk. Replacement of 3T HCUs manufactured before September 2014 with new devices of the same or other brands can be considered as a mitigating strategy. However, it should be noted that the potential risks associated with other models remain to be defined.

Centres using 3T HCUs should strictly follow the instructions for use, and in particular those for cleaning and decontamination, issued by the manufacturer. Establishing a quality control process with written procedures including traceability of the HCU used in each operation is also advisable.

Healthcare providers (including cardiologists, pulmonologists, rheumatologists, infectious disease specialists, ophthalmologists, haematologists and primary care providers) caring for patients who have undergone open-heart surgery or other surgery involving cardiopulmonary bypass, such as heart and/or lung transplantation, should be vigilant for cases of endocarditis or other cardiovascular, deep surgical site, or disseminated infection that are of unidentified origin. They should also be vigilant for other granulomatous disease, including those with the characteristics of sarcoidosis, and consider testing such cases specifically for slow-growing NTM, such as *M. chimaera*.

Other measures that EU/EEA countries may consider include informing patients who have undergone open-heart surgery involving exposure to 3T HCUs before the implementation of mitigation measures about the risk of acquisition and the signs and symptoms of infections with NTM, and in particular *M. chimaera*. This is especially important if they were operated on in a centre that detected a case of *M. chimaera* previously. Accessible information should be readily available for healthcare providers and patients.

Suggested citation: European Centre for Disease Prevention and Control. Invasive cardiovascular infection by *Mycobacterium chimaera* associated with 3T heater-cooler system used during open-heart surgery – 18 November 2016. Stockholm: ECDC; 2016.

EX. B

This information could be online, disseminated in the form of a letter to the patient, a patient information leaflet, or as frequently asked questions (FAQ).

An ECDC protocol is available for retrospective case detection, laboratory diagnosis and environmental testing of *Mycobacterium chimaera*. Clinical and mycobacterial diagnostic investigations should be available and accessible for patients at risk after cardiovascular surgery to ensure prompt diagnosis and treatment. Microbiological testing of water and air samples for the detection of *M. chimaera* and other NTM is technically challenging, with a high likelihood of false negative results. Nevertheless, clinical vigilance, prospective case detection and notification of invasive cardiovascular infection caused by *M. chimaera* after open-heart surgery, as well as selective environmental testing, may be considered in the coming years in order to monitor the effectiveness of control measures, and ensure timely diagnosis and treatment for infected patients.

Regulatory bodies in charge of licensing and agencies monitoring the safety of such devices should be aware of the association of invasive cardiovascular infections caused by *M. chimaera* and other NTM with HCUs and options for regulatory action should be considered. Relevant information should be disseminated to all centres performing open-heart surgery or other surgery involving extracorporeal circulation. Devices containing water circuits or using water during operation or maintenance and used in sensitive clinical areas should be carefully evaluated for the risk of contamination by NTM.

Source and date of request

ECDC internal decision, 11 November 2016.

Public health issue

Update the assessment of risk of invasive cardiovascular infection by *Mycobacterium chimaera* associated with heater-cooler units used during open-heart surgery in Europe.

Consulted experts

External experts: Benedetta Allegranzi (World Health Organization, Switzerland), Anne Berger Carbonne (Public Health France), Karen Burns (Health Protection Surveillance Centre, Ireland), Meera Chand (Public Health England), Ana Paula Coutinho Rehse (WHO Regional Office for Europe, Denmark), Sebastian Haller (Robert Koch Institute, Germany), Jakko van Ingen (Radboud University Medical Centre, the Netherlands), Theresa Lamagni (Public Health England), Hugo Sax (University Hospital Zurich, Switzerland), Nahoko Shindo (World Health Organization Switzerland), Sara Tomczyk (World Health Organization, Switzerland), Elsebeth Tvenstrup Jensen (Statens Serum Institut, Denmark)

ECDC experts: Margot Einöder-Moreno, Diamantis Plachouras, Dominique Monnet, Marc Struelens, Anna-Pelagia Magiorakos, Anke Kohlenberg, Denis Coulombier.

Disease background information

Mycobacterium chimaera is a slow-growing non-tuberculous mycobacterium (NTM) that was identified as a species within the *Mycobacterium avium* complex in 2004 [1]. Identification requires molecular diagnostic testing. *Mycobacterium chimaera* has been associated with lung infections in patients with underlying lung disease, such as chronic obstructive pulmonary disease. Colonisation of water sources and systems, with formation of biofilm is possible.

In 2014, airborne transmission of *M. chimaera* from heater-cooler units (HCUs) was reported for the first time. HCUs are used to regulate the temperature of the blood, and of the cardioplegia solution during extracorporeal circulation, and use filtered water as a heat exchanger [2]. Water is contained in tanks and circulated through a closed circuit to the heart-lung unit. The device is connected to the membrane oxygenator through tubing and is usually situated in the operating room. The water in the circuit does not come into contact with the patient, but the circuit is not airtight and cooling of the water is accomplished with a fan.

Event background information

This section includes information from published reports, as well as unpublished information communicated through the Early Warning and Response System (EWRS), the Epidemic Intelligence Information System (EPIS) platform, during teleconferences and from a survey of the affected EU/EEA countries.

Since 2011, cases of invasive cardiovascular infection caused by *M. chimaera* have been reported in patients who had previously undergone open-heart surgery using HCUs in seven EU/EEA countries. In April 2015, ECDC published a rapid risk assessment on the potential risk of invasive cardiovascular infection by *M. chimaera* associated with the use of HCUs [3], which this document is an update of in view of accumulating new evidence.

Case detection

Since 2011, 52 cases of post-surgical cardiovascular infection caused by *M. chimaera* have been reported in Europe: France (two cases), Germany (five cases), Ireland (four cases), the Netherlands (four cases), Spain (one case), UK (25 cases), and Switzerland (10 cases). Ten deaths have been reported to date among these patients but not all deaths were attributed to the infection. Cases have also been reported in the US, Canada, Australia and Hong-Kong Special Administrative Region [4-10].

In the majority of cases, patients had undergone cardiac valve replacement/reconstruction, and/or the insertion of an aortic vascular graft in the five years prior to diagnosis. Patients who have undergone other operations that involve cardiopulmonary bypass, including heart and/or lung transplantation, or introduction of ventricular assist devices (VAD), are also at risk [11].The majority of infections were endocarditis, graft infection and disseminated infection, but cases of sternal osteomyelitis have also been reported. Disseminated infection can be indolent, with diverse presentations, such as bacteraemia, granulomatous hepatitis, nephritis, splenomegaly, chorioretinitis, osteomyelitis and bone marrow involvement with cytopenia [12] and may mimic sarcoidosis. The reported interval from operation to infection ranges from three months to five years, with a median interval of 19 months [13]. These infections are difficult to treat, requiring combination antimicrobial therapy and surgical intervention, and have a high rate of treatment failure and fatal outcome [12].

Denmark, France, Hungary, Ireland, the Netherlands, Norway, Sweden, and the UK have done retrospective and/or prospective case finding (e.g. through hospital patient registries and laboratories, physician notification and awareness raising for increased diagnostic testing of possible cases). The retrospective case finding went back from five years (Denmark, France, Sweden, one hospital in Norway) to 13 years (Ireland).

Denmark, Norway, Hungary and Sweden did not detect any case through active case finding. No case has been notified in Austria, Slovakia, Latvia and Poland, but active case finding has not been performed. No data are available from case finding or environmental investigation in other Member States.

To date, no cases of post-operative invasive infection caused by *M. chimaera* associated with 3T HCUs manufactured after September 2014 have been reported.

Environmental testing

Investigators in Denmark, France, Ireland, the Netherlands, Sweden, Switzerland and the UK performed microbiological testing of HCUs for *Mycobacterium chimaera*, and 3T devices contaminated with *M. chimaera* were identified in all of them. In Slovakia, samples taken from HCUs were negative for *M. chimaera*. In the UK, the Netherlands, Sweden and Switzerland, some HCUs tested positive for *M. chimaera* after decontamination by the manufacturer. In Scotland, *M. chimaera*-contaminated 3T HCUs were identified that had been manufactured after September 2014.

Denmark, France, Germany, Ireland, the Netherlands and the UK have performed whole-genome sequencing of the isolates. Results are pending.

Of note, all cases of invasive cardiovascular infection by *M. chimaera* reported until now have been associated with the use of 3T HCUs. Culture of air samples from the operating room when these 3T HCUs were in use, have grown *M. chimaera*, indicating that these HCUs were responsible for the production of bio-aerosols [2,14,15], making airborne transmission the most probable route. Devices from other manufacturers have also been found to be contaminated by *M. chimaera* and other microorganisms in Denmark, the Netherlands and Germany. However, to date, results from investigations of air contamination associated with these other HCUs are not available.

Contamination of HCUs used in extracorporeal membrane oxygenation (ECMO) was also detected. However, this was not associated with contamination of the air surrounding the devices, possibly because the water circuits of these devices are airtight. To date, no infections have been linked to the use of ECMOs [2,16].

Contamination of HCUs with other waterborne pathogens, including other NTM (e.g. *M. chelonae, M. gordonae, M. fortuitum* or *M. scrofulaceum, M. gordonae, M. kansasii* and *M. lentiflavum), Legionella* spp., non-fermenting Gram-negative bacteria and fungi has also been detected and is of concern, although until now only one case of sternal wound infection by *Legionella* spp. has been reported in Switzerland. The variety of different pathogens identified in HCUs also indicates a risk of contamination within hospitals. Further investigations into the association of HCUs with infections by these pathogens are required to address this risk.

Risk mitigation measures

The most likely source of *M. chimaera* infection were 3T HCUs contaminated at the production site during the manufacturing process [4,17,18] according to epidemiological and microbiological investigations of clinical and environmental isolates from Europe and the US, which are supported by preliminary results from whole-genome sequencing comparative analysis. The investigations also found that 3T HCU-produced aerosols with *M. chimaera* can reach the operating table despite ultraclean air ventilation [14,19].

In August 2014, the manufacturer of 3T HCUs implemented a device disinfection process of new devices prior to shipment [20] among other measures.

Testing conducted by the manufacturer in August 2014 found *M. chimaera* contamination on the production line and water supply at the 3T manufacturing facility. The 3T devices manufactured at this facility were distributed worldwide. In response to the M. chimaera findings in August 2014, the manufacturer added cleaning and disinfection procedures to the production line in September 2014.

In September 2014, in response to *M. chimaera* contamination of 3T HCUs, the manufacturer introduced a modification in the post-production process, updated the instructions for use and issued relevant field safety notices, with a last update on 13 October 2016 [21]. The updated instructions address decontamination and enhanced maintenance protocols of 3T HCUs. A deep-cleaning process is also provided by the manufacturer. However, although the modified instructions have been associated with a decrease in colony counts [22,23], eradication of *M. chimaera* has not been consistent. In addition, the Food and Drug Administration (FDA) reported on *M. chimaera*-contaminated 3T HCUs produced after September 2014, although it is unknown whether these were contaminated at the manufacturing site or at the healthcare facility where they were used.

In April 2015, ECDC published a Rapid Risk Assessment on the potential risk of invasive cardiovascular infection by M. chimaera associated with the use of HCUs [3], and in August 2015, a protocol for case detection, laboratory diagnosis and environmental testing of Mycobacterium chimaera [24].

The US Centers for Disease Control and Prevention published a guidance document for health departments, health care facilities and providers, and patients [25]. The Food and Drug Administration recommended immediate device removal if any 3T HCU, accessory or component tests were positive for *M. chimaera* or were associated with cases of *M. chimaera* infection; and to strongly consider transitioning away from use of 3T HCUs manufactured before September 2014 until the manufacturer has implemented risk-mitigation strategies, limiting their use to emergency and/or life threating situations if no other HCU is available [26].

National regulatory authorities for medical devices have been notified across Europe, and a number of control measures have been implemented. The manufacturer's cleaning and disinfection protocol is being used as a basis for local protocols. Several national authorities have recommended removing the HCUs from the operating rooms, and this has been implemented in some countries such as Denmark, Ireland, France and the Netherlands. However, in Germany and the UK, practical difficulties were encountered that prevented the full implementation of this this measure (e.g. the length of the tubing required to connect to the membrane oxygenator).In many cases the HCUs have been placed as far from the patient as possible, with the HCU exhaust directed away from the operating table andor to the exhaust outlet of the room air ventilation system. Custom-made housing for 3T HCUs was also designed and implemented in Denmark and Switzerland. In some hospitals in Norway, HCUs were outside of the operating room placed from the beginning. The University Hospital Zurich designed custom-built special housing for the 3T HCU connected to the air exhaust of the operating theatre, an intervention that was expensive and technically demanding [22].

National health authorities have notified a broad panel of clinicians, scientific and professional societies about the risk of invasive infection by *M. chimaera* associated with HCUs, through meetings, articles and letters or documents. Information for patients and the public has also been provided in the form of information leaflets and press releases [13,27,28].

There is limited information on the effectiveness of patient notification. From the experience of one hospital in the U.S., almost 200 patients could not be reached by phone among 1 500 exposed patients. Among the patients that were notified, 131 underwent evaluation at an 'NTM' clinic, without any cases being detected. Two cases at the same hospital were identified through healthcare provider notification [29].

ECDC threat assessment for the EU

The risk of invasive infection by *M. chimaera* in patients having undergone open-heart surgery has been estimated to be 0.4 – 16 per 10 000 patient-years [2,13]. Given a background risk of 1.2% for surgical site infection in the first year after cardiac valve operations, and a cumulative 5-year incidence of prosthetic valve endocarditis of 3.2–5.7% [30], the risk of invasive infection by *M. chimaera* is considered low. However, this risk is likely to be underestimated due to the long interval between operation and diagnosis, as well as the technical difficulty of diagnosing this infection. Decisions to delay surgery until this risk is mitigated should take into account the risk of delaying surgery on an individual basis for each patient.

The manufacturer introduced risk mitigation measures in September 2014, including updated cleaning and disinfection procedures and modifications of the production line. Isolation of NTM from 3T HCUs manufactured after September 2014 indicate that the risk has not yet been eliminated [2,19,26]. To date, there have been no reported cases of *M. chimaera* infection associated with 3T HCUs manufactured after September 2014.

The risk of infection by *M. chimaera* and other pathogens associated with HCUs other than the 3T remains unknown, but is plausible and depends on the potential for aerosol formation. Further study of HCUs and other devices containing water circuits and used in surgery and other sensitive clinical areas need to be performed to inform the estimation of this risk.

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EXHIBIT C

Important Information Letter

SORIN GROUP
AT THE HEART OF MEDICAL TECHNOLOGY

SORIN GROUP DEUTSCHLAND GMBH · Lindberghstr. 25 · D-80939 München

«Name1»
«Name2»
«Name3»
«Address»
«Address»

IMPORTANT INFORMATION
Cardiac Surgery Mycobacterium Risks
Disinfection and Cleaning of Sorin Heater Cooler Devices

Date:	14. July 2014
Reference No:	IIS 9611109-07-14-14
Attention:	**Hygiene Specialists, Cardiac Surgery Operating Room Responsible,** Risk/ Safety Managers, Distributors, Clinicians, Perfusionist and other users of these devices
Reason:	Disinfection and cleaning of Heater Cooler Units

Dear Valued Customer,

We would like to bring to the attention of our customers a newly identified risk for cardiac surgery patients. Some cardiac surgery patients have been infected with a slow growing *Mycobacterium chimaera*. This risk was identified during investigations into these patient infections, root cause investigations are ongoing. Sorin takes the on-going investigations very serious and is participating with Swissmedic, Swiss Federal Office of Public Health, Swissnoso and the hospital where an in depth investigation is actually carried out. This risk is difficult to identify as current practices for monitoring the contamination of a cardiac surgery theatre may not identify the slow growing, chemically resistant organisms involved. *Mycobacteria* organisms are found in water, including tap water sources. Please find additional information on *Mycobacteria* in Attachment 1.

It is important to assure that your staff is aware of the *Mycobacteria* risk and to review your hygiene & surgical practices in the cardiac surgery theatre. This review should include your sampling and monitoring programs for your water sources, solution preparations and systems that use water in the cardiac surgery theatre. Among these water systems, heater cooler device(s) need strict adherence to the cleaning, disinfection and maintenance according to the operating manual (for Sorin devices, see Attachment 2). Without vigilant performance of the disinfection per the *Operating Instructions,* these organisms can multiply in a heater cooler device and potentially form biofilm. As you are aware, the water in the heater cooler devices is not intended to

SORIN GROUP
DEUTSCHLAND GMBH
Lindberghstr. 25 · D-80939 München
T.: +49-(0)89-323 01 0
F.: +49-(0)89-323 01 100
www.sorin.com

Geschäftsführer:
Alexander H. J. Neumann
Giulio Cordano

Amtsgericht München
HRB 100852
USt-IdNr. (VAT) DE 129304291
Steuer-Nummer: 143/181/70429

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have direct contact with the patient. One of the highest risks of contamination for the patient is a direct contact transfer of water/solution droplets containing *Mycobacteria* into the surgical field. Another risk that should be reviewed, is the air distribution within the cardiac surgery theatre as this can be a transmission method for *Mycobacteria*. The air conditioning as well as ventilation units including the heater cooler device fans need to be considered in that analysis.

During the investigation work it has been identified that some hospitals heater cooler devices are contaminated. By way of caution and as a safety measure, Sorin reminds its customers using heater cooler devices about the importance of adhering to the correct maintenance of the device at all times and in particular to assure that the cleanliness of the water in the device is maintained. If the water is not properly disinfected and maintained, microbiological growth can occur within the device and over time biofilm may form. We enclose hereto our latest version of the operating instructions for the 3T Heater Cooler Devices giving clear guidance on how the cleanliness of the water in the device is to be maintained. Please note that strict adherence to the instructions is mandatory for the safe use of the device.

You may continue to safely use the heater cooler devices in accordance with the Operator's Manual.

Recommendations:

- Review this information to assure that you are aware of proper water management in your cardiac surgery theatre. Specifically, assure that your team understands *Mycobacteria* and the potential contamination risks for cardiac surgeries. Introductory information is provided in Attachment 1.
- Review your heater cooler operating practices and cardiac surgery theatre water management practices. Also evaluate your heater cooler device(s) for potential contamination.
- Refer to the heater cooler device operator's manual and/or Attachment 2 and review the necessary disinfection practices to assure your practices are aligned with the directions.
- If you are concerned that your vigilance to the operating instructions may be in question, perform microbiological sampling of the water in your heater cooler device, disinfect the device and determine if decontamination is necessary.

Please complete and return the attached Confirmation Form (see Attachment 3) by fax to «Number» or by email to «E-mail Address».

Distribution of this Information:

Please assure this Important Information is distributed to all personnel who needs to be aware of this information. If you have transferred the affected products to a third party, please pass this information to them as well as informing Sorin Group Deutschland GmbH at +49 89 323 01 152 of the transfer.

A copy of this documentation has been provided to the appropriate Regulatory Agencies and they are aware of this measure by Sorin.

SORIN GROUP
DEUTSCHLAND GMBH
Lindberghstr. 25 · D-80939 München
T.: +49-(0)89-323 01 0
F.: +49-(0)89-323 01 100
www.sorin.com

Geschäftsführer:
Alexander H. J. Neumann
Giulio Cordano

Amtsgericht München
HRB 100852
USt-IdNr. (VAT) DE 129304291
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Contact reference person:

If you have any further questions please feel free to contact us. We will not fail to inform you in due course once further information particularly with regard the root cause of the observed infections are obtained.

For questions regarding this Important Information, please contact Christian Peis, Director QA, Sorin Group Deutschland GmbH at +49 89 323 01 152, via fax at +49 89 323 01 333 or via e-mail at SGD.fsca@sorin.com.

Thank you for your cooperation in this matter. Sorin Group is committed to provide quality products and service to its customers.

Sincerely,

i.V. Christian Peis
Director Quality Assurance Cardiopulmonary BU
Sorin Group Deutschland GmbH

Enclosures:
Attachment 1: Mycobacterium Data Sheet
Attachment 2: Disinfection Excerpt from the Operating Instructions for 3T Heater Cooler
Attachment 3: Customer Response Form

SORIN GROUP
DEUTSCHLAND GMBH
Lindberghstr. 25 · D-80939 München
T.: +49-(0)89-323 01 0
F.: +49-(0)89-323 01 100
www.sorin.com

Geschäftsführer:
Alexander H. J. Neumann
Giulio Cordano

Amtsgericht München
HRB 100852
USt-IdNr. (VAT) DE 129304291
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Attachment 1
Mycobacterium Data Sheet:
IMPORTANT INFORMATION

Sorin Heater Cooler Devices - Mycobacterium
Reference # IIS 9611109-07-14-14

FOR GENERAL HEALTHCARE STAFF - INTRODUCTION

- Mycobacteria are widely distributed in the ecosystem, are present in water, and even survive in chlorinated drinking water. Some species are classic human pathogens, for example *M. tuberculosis* that causes TB. However, most mycobacteria are not considered harmful to humans. These environmental mycobacteria are termed nontuberculous mycobacteria (NTM). These do occasionally cause opportunistic infections. (Van Ingen, J Med Microbiol, September 2012 vol. 61 no. Pt 9, 1234-1239).
- For example, *M. chimaera* was identified as the causative agent of a respiratory tract infection in patients with cystic fibrosis. (Cohen-Bacrie et al. Journal of Medical Case Reports 2011, 5:473).
- The various NTM species have greatly differing microbiological culture requirements and infective characteristics. Special methods must be employed to determine presence or absence and to obtain accurate identification.
- In order to control these organisms in medical environments and equipment, it is critical to identify effective chemicals against NTM and follow Instructions for Use provided by the manufacturer of disinfectants and medical equipment/devices.
- Particular attention **must** be paid to the use of water in critical health care situations because water that is not sterilized, for example by filtration, often carries these kinds of bacteria.

MYCOBACTERIA ARE INHERENTLY RESISTANT TO CHEMICAL DISINFECTANTS AND ANTIBIOTICS

- Mycobacteria have a natural resistance to many disinfectants. All mycobacteria share a characteristic cell wall, which is thicker than in most bacteria, which is hydrophobic, waxy, and rich in mycolic acids. This cell wall makes a substantial contribution to the environmental and chemical tolerance of this group. http://www.cdc.gov/hicpac/Disinfection_Sterilization/4_0efficacyDS.html

FOR TECHNICAL & MEDICAL STAFF - MYCOBACTERIA REQUIRE SPECIALIZED MICROBIOLOGY

- Mycobacteria require specialized growth media and techniques for successful culture. Therefore, they may be present in the samples and not detected due to the inadequate culture media or incubation periods. Extension of incubation for up to 60 days or more may be required to recover these types of isolates.
- Sampling for these organisms can be made challenging by their highly hydrophobic nature. For sampling surfaces directly, or via a liquid medium, swabbing vigorously to recover these organisms may be needed. Also, using a surfactant (e.g. Tween) can assist in recovering during sampling and manipulation during culture/testing.
- It is likely that the presence of these NTM can be overlooked by routine medical microbiological and environmental testing.
- Sampling of the environment (air and surfaces), equipment, and clinical specimens, should be considered whenever mycobacterial infection is a risk. This can include water filled equipment in health care settings. For general mycobacteriology see: http://www.health.gov.au/internet/main/publishing.nsf/Content/cda-cdi3001-pdf-cnt.htm/$FILE/cdi3001f.pdf For detailed on NTM information see: https://www.thoracic.org/statements/resources/mtpi/nontuberculous-mycobacterial-diseases.pdf

SORIN GROUP
DEUTSCHLAND GMBH
Lindberghstr. 25 · D-80939 München
T.: +49-(0)89-323 01 0
F.: +49-(0)89-323 01 100
www.sorin.com

Geschäftsführer:
Alexander H. J. Neumann
Giulio Cordano

Amtsgericht München
HRB 100852
USt-IdNr. (VAT) DE 129304291
Steuer-Nummer: 143/181/70429

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Attachment 2
Operating Instructions Excerpt:

Cleaning and Disinfection of the Heater Cooler Device

IMPORTANT INFORMATION

Sorin Heater Cooler Devices - Mycobacterium
Reference # IIS 9611109-07-14-14

The following chapters are attached from the current Operating Manual GA-16-XX-XX ENG (rev 11) of the 3T heater cooler device.

5.2 Filling the water tanks

6.2 Cleaning and disinfection of the housing

6.2.1 Disinfection of the water circuits

6.2.2 Protecting the water circuits from microbial growth

SORIN GROUP
DEUTSCHLAND GMBH
Lindberghstr. 25 · D-80939 München
T.: +49-(0)89-323 01 0
F.: +49-(0)89-323 01 100
www.sorin.com

Geschäftsführer:
Alexander H. J. Neumann
Giulio Cordano

Amtsgericht München
HRB 100852
USt-IdNr. (VAT) DE 129304291
Steuer-Nummer: 143/181/70429

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Attachment 3
Customer Response Form

IMPORTANT INFORMATION

Sorin Heater Cooler Devices - Mycobacterium

Reference # IIS 9611109-07-14-14

According to our records you have the following impacted products:

<< Fill in the customer related codes and serial numbers only- Use Product Trace list (Excel File)>>

Product Code	Product description	Serial Number

Please return this completed form to:

Sorin Site/ Distributor Name: <<Print Your Company name here>>
Country: <<Print Your Country here>>
Contact Name: << Print Your Contact Name here>>
E-mail: <<Print Your E-mail address here>>
Fax No.: <<Print Your Fax No. here>>
Phone Number: <<Print Your Phone No. here>>

Section 1 - Please Complete:

1. We HAVE reviewed and understand the attached Important Information ☐
2. Yes- We do have the listed affected products and we will follow the instruction ☐
3. We DO NOT understand the attached Important Information and request more information ☐

Please contact us:
Christian Peis, Director QA, Sorin Group Deutschland GmbH at +49 89 323 01 152, via fax at +49 89 323 01 333 or via e-mail at SGD.fsca@sorin.com

Customer Name: <<Print Your Company name here>>
Country: <<Print Your Country here>>
Contact Name: << Print Your Contact Name here>>
E-mail: <<Print Your E-mail address here>>
Fax No.: <<Print Your Fax No. here>>
Phone Number: <<Print Your Phone No. here>>

Submitted by ……..
Signature ……..
Date …...../……...../……

SORIN GROUP
DEUTSCHLAND GMBH
Lindberghstr. 25 · D-80939 München
T.: +49-(0)89-323 01 0
F.: +49-(0)89-323 01 100
www.sorin.com

Geschäftsführer:
Alexander H. J. Neumann
Giulio Cordano

Amtsgericht München
HRB 100852
USt-IdNr. (VAT) DE 129304291
Steuer-Nummer: 143/181/70429

EX. C

EXHIBIT D
MAUDE Adverse Event Report

MAUDE Adverse Event Report: SORIN GROUP USA STOCKERT - SORIN 3T HEATER COOLER

SORIN GROUP USA STOCKERT - SORIN 3T HEATER COOLER

Back to Search Results

Model Number 3T
Event Type Death
Event Description

The 15 pts have tested positive +afb for an atypical mycobacterium infection. All infections have been surgical site infections. The investigation is still on-going. The common denominator for the cardiac surgeries is the profusion machine. The machine has been cultured and found to have the mycobacterium in the water. The machine was pulled from service (b)(6) 2014. The terumo health exchanger was being used on the machine. (b)(6) has increased the frequency of the vendor's recommendation for disinfection from every two weeks to weekly. Out of the 15 pts that were infected, 4 have expired. The infections were thought to be a contributing factor, yet all pts had major, underlying existing and significant medical conditions. Several pts in the hosp presented with post-operative wound infections caused by an unusual organism, atypical mycobacterium. It has been determined that a total of 15 pts who had surgery were infected. The investigation is still on-going and the exact etiology is still unk. A common factor for many of the pts infected is the sorin profusion machine.

Search Alerts/Recalls[22]

New Search | Submit an Adverse Event Report[23]

Brand Name STOCKERT - SORIN 3T HEATER COOLER
Type of Device 3T HEATER COOLER
Manufacturer *(Section D)* SORIN GROUP USA
14401 W 65th Way
Arvada CO 80004
MDR Report Key 3984530
Report Number 3984530
Device Sequence Number 1
Product Code DWC[24]
Report Source User Facility
Reporter Occupation RISK MANAGER
Type of Report Initial
Report Date 08/01/2014
***1* Device Was Involved in the Event**
***1* Patient Was Involved in the Event**
Date FDA Received 08/06/2014
Is This An Adverse Event Report? No
Is This A Product Problem Report? Yes
Device Operator Service Personnel
Device MODEL Number 3T
Device Catalogue Number 16-02-85
Is The Reporter A Health Professional? Yes
Distributor Facility Aware Date 06/05/2014
Device Age 2 yr
Date Report TO Manufacturer 06/19/2014
Is this a Reprocessed and Reused Single-Use Device? No

Patient TREATMENT DATA
Date Received: 08/06/2014 Patient Sequence Number: 1

Links on this page:

1. http://www.addthis.com/bookmark.php?u508=true&v=152&username=fdamain
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10. /scripts/cdrh/cfdocs/cfMAUDE/TextSearch.cfm
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12. /scripts/cdrh/cfdocs/cfPMA/pma.cfm
13. /scripts/cdrh/cfdocs/cfHDE/hde.cfm
14. /scripts/cdrh/cfdocs/cfPCD/classification.cfm
15. /scripts/cdrh/cfdocs/cfStandards/search.cfm
16. /scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm
17. /scripts/cdrh/cfdocs/cfPCD_RH/classification.cfm
18. /scripts/cdrh/cfdocs/cfAssem/assembler.cfm
19. /scripts/cdrh/cfdocs/Medsun/searchReportText.cfm
20. /scripts/cdrh/cfdocs/cfClia/Search.cfm
21. /scripts/cdrh/cfdocs/cfTPLC/tplc.cfm
22. https://www.fda.gov/MedicalDevices/Safety/ListofRecalls/default.htm
23. https://www.accessdata.fda.gov/scripts/medwatch/
24. ../cfPCD/classification.cfm?start_search=&ProductCode=DWC

Page Last Updated: 07/31/2017

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FDA

U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
Ph. 1-888-INFO-FDA (1-888-463-6332)
Contact FDA

USA.gov

For Government For Press

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EX. D

U.S. Department of Health & Human Services

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8. /scripts/cdrh/cfdocs/cfpmn/denovo.cfm
9. /scripts/cdrh/cfdocs/cfRL/rl.cfm
10. /scripts/cdrh/cfdocs/cfMAUDE/TextSearch.cfm
11. /scripts/cdrh/cfdocs/cfRES/res.cfm
12. /scripts/cdrh/cfdocs/cfPMA/pma.cfm
13. /scripts/cdrh/cfdocs/cfHDE/hde.cfm
14. /scripts/cdrh/cfdocs/cfPCD/classification.cfm
15. /scripts/cdrh/cfdocs/cfStandards/search.cfm
16. /scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm
17. /scripts/cdrh/cfdocs/cfPCD_RH/classification.cfm
18. /scripts/cdrh/cfdocs/cfAssem/assembler.cfm
19. /scripts/cdrh/cfdocs/Medsun/searchReportText.cfm
20. /scripts/cdrh/cfdocs/cfClia/Search.cfm
21. /scripts/cdrh/cfdocs/cfTPLC/tplc.cfm
22. https://www.fda.gov/MedicalDevices/Safety/ListofRecalls/default.htm
23. https://www.accessdata.fda.gov/scripts/medwatch/
24. ../cfPCD/classification.cfm?start_search=&ProductCode=DWC

EX. D

EXHIBIT E
FDA June 1, 2016 Safety Communication

Archived Content

The content on this page is provided for reference purposes only. This content has not been altered or updated since it was archived.

Mycobacterium chimaera Infections Associated with Sorin Group Deutschland GmbH Stöckert 3T Heater-Cooler System: FDA Safety Communication

FDA issued an **updated safety communication (/MedicalDevices/Safety/AlertsandNotices/ucm520191.htm)** on October 13, 2016.

June 1, 2016

Audiences

- Health care providers who use 3T Heater-Cooler System
- Primary care providers who are responsible for the ongoing care of patients who have undergone cardiothoracic surgery
- Patients who have undergone cardiothoracic surgery
- Hospital staff who are responsible for operating and maintaining 3T Heater-Cooler System

Medical Specialties

Cardiothoracic Surgeons, Cardiovascular Surgeons, Orthopedic Surgeons, Neurosurgeons, General Surgeons, Anesthesiologists, Infection Control, Infectious Disease Physicians, Pediatrics, Primary Care, and Intensive Care Physicians

Product

The Stöckert 3T Heater-Cooler System (3T), manufactured by Sorin Group Deutschland GmbH is intended to provide temperature-controlled water to 1) oxygenator heat exchangers, 2) cardioplegia (paralysis of the heart) heat exchangers, and/or 3) warming/cooling blankets to warm or cool a patient during cardiopulmonary bypass procedures lasting six hours or less

EX. E

Purpose

The FDA is providing new information about *Mycobacterium chimaera* (*M. chimaera*) infections associated with the use of the 3T in patients who have undergone cardiothoracic surgeries.

Summary of Problem and Scope

Heater-cooler devices (/MedicalDevices/ProductsandMedicalProcedures/CardiovascularDevices/Heater-CoolerDevices/ucm20082725.htm) are commonly used during cardiothoracic surgeries, as well as other medical and surgical procedures, to warm or cool a patient in order to optimize medical care and improve patient outcomes. Heater-cooler devices include water tanks that provide temperature-controlled water to external heat exchangers or warming/cooling blankets through closed circuits. Although the water in the circuits does not come into direct contact with the patient, there is the potential for contaminated water to enter other parts of the device or to aerosolize, transmitting bacteria through the air and through the device's exhaust vent into the environment and to the patient.

In October 2015, the FDA issued a **Safety Communication (/MedicalDevices/Safety/AlertsandNotices/ucm466963.htm)** to provide recommendations to minimize patient risk to infections associated with heater-cooler devices. Since issuing this communication, the FDA has continued to evaluate the causes and risk factors for transmission of microbial agents associated with heater-cooler devices and is collaborating with professional societies, public health partners, and experts to develop strategies to minimize patient exposure.

A recently published European study[1] describes a link between *M. chimaera* clinical samples from several infected cardiothoracic patients with samples from the heater-cooler devices used during these patient's procedures, and with environmental samples from the device manufacturer's production and servicing facility in Germany. The results of this paper suggest a direct link between the *M. chimaera* to which the European patients were exposed and became infected during open-chest cardiac surgery, and one specific heater-cooler model – the 3T.

M. chimaera is a type of nontuberculous mycobacterium (NTM) that may cause serious illness or death. FDA believes these NTM infections associated with the 3T are rare. However, they are difficult to detect because patients infected with *M. chimaera* may not develop symptoms and signs of infection for months to years after initial exposure.

Testing conducted by the manufacturer in August 2014 found *M. chimaera* contamination on the production line and water supply at the 3T manufacturing facility. Units from this facility can be found worldwide. In response to the *M. chimaera* findings in August 2014, the manufacturer added cleaning and disinfection procedures to the production line in September 2014. Samples taken at the same manufacturing facility in June 2015 did not show *M. chimaera* on the production line, potentially eliminating the production line as a contamination source.

The FDA has received reports of U.S. patients infected with *M. chimaera* after undergoing cardiothoracic surgery that involved the use of the 3T. Currently, efforts are underway in the U.S. to determine if the infections in U.S. patients and *M. chimaera* isolates from samples taken from the 3T are linked with *M. chimaera* isolates from European patients who were infected and the *M. chimaera* previously identified at the 3T manufacturer's production and servicing facility in Germany.

The FDA's recommendations are based on currently available information about *M. chimaera* infections associated with the 3T. During the upcoming June 2-3, 2016 **Circulatory System Devices Panel of the Medical Devices Advisory Committee meeting (https://www.federalregister.gov/articles/2016/04/15/2016-08737/circulatory-system-devices-panel-of-the-medical-devices-advisory-committee-notice-of-meeting)**, the FDA will review

available data and seek expert scientific and clinical opinion related to all heater-cooler device contaminations, associated patient infections, and mitigation strategies. As new and important information becomes available, the FDA will evaluate the information and update its recommendations, as appropriate.

Recommendations for Health Care Facilities and Staff

In addition to the recommendations provided in the 2015 **Safety Communication (/MedicalDevices/Safety/AlertsandNotices/ucm466963.htm)** for facilities and staff using heater-cooler devices, the FDA recommends the following:

- If your facility purchased and used the 3T prior to September 2014, be aware the units may have been shipped from the factory contaminated with *M. chimaera*. Such facilities should:
  - inform health care providers who have performed cardiothoracic surgeries, that there is a possibility that their patients may have been infected with *M. chimaera*. Reports to date suggest there may be a higher risk of patient infection associated with surgeries that introduced a prosthetic product/material [e.g., heart valve, graft, LVAD], or heart transplants when the 3T was used.
  - determine a method for patient follow-up and establish patient surveillance in cases of potential exposure, per the recommendations in CDC's **Interim Guide for the Identification of Possible Cases of Nontuberculous Mycobacterium Infections Associated with Exposure to Heater-Cooler Units (http://www.cdc.gov/hai/pdfs/outbreaks/Guide-for-Case-Finding.pdf)**.
- If you purchased and used the 3T after September 2014:
  - continue to follow the recommendations provided in FDA's 2015 **Safety Communication (/MedicalDevices/Safety/AlertsandNotices/ucm466963.htm)** and the manufacturer's most current Instructions for Use for cleaning, disinfecting and maintenance to reduce the risk to patients.

During the upcoming June 2-3, 2016 **Circulatory System Devices Panel of the Medical Devices Advisory Committee meeting (https://www.federalregister.gov/articles/2016/04/15/2016-08737/circulatory-system-devices-panel-of-the-medical-devices-advisory-committee-notice-of-meeting)**, the FDA will seek expert clinical opinion and recommendations for patient notification and patient follow-up procedures. Recommendations for sampling and monitoring of the 3T and other heater-cooler devices will also be discussed. As new and important information becomes available, the FDA will evaluate the information and update its recommendations, as appropriate.

Recommendations for Patients

- Be aware that:
  - in the U.S., cardiopulmonary bypass procedures involve the use of a heater-cooler device.
  - the FDA has received reports of patient infections associated with exposure to *M. chimaera* when a contaminated 3T (heater-cooler device) was used during surgery.
  - there may be an increased risk of infection if you received a heart valve, graft, LVAD or any other prosthetic product/material or had a heart transplant.
  - during the upcoming June 2-3, 2016 **Circulatory System Devices Panel of the Medical Devices Advisory Committee meeting (https://www.federalregister.gov/articles/2016/04/15/2016-08737/circulatory-system-devices-panel-of-the-medical-devices-advisory-committee-notice-of-meeting)**, the FDA will seek clinical opinion about the risk of patient infection with NTM associated with the use of heater-cooler devices and mitigation strategies. As new and important information becomes available, the FDA will evaluate the information and update its recommendations, as appropriate.

EX. E

- If you have undergone cardiopulmonary bypass, be aware of the possible signs and symptoms of NTM infection. These may include:
  - fatigue
  - difficulty breathing
  - persistent cough or cough with blood
  - fever
  - pain
  - redness, heat, or pus at the surgical site
  - muscle pain
  - joint pain
  - night sweats
  - weight loss
  - abdominal pain
  - nausea
  - vomiting
- If you have undergone a cardiopulmonary bypass procedure and are experiencing any of the signs and symptoms of NTM infection as outlined above, contact your health care provider as soon as possible.
- If you are not currently experiencing any changes in your general health, inform your health care provider during your next wellness visit that you have undergone a cardiopulmonary bypass procedure to determine if you require further testing or monitoring for possible exposure to NTM.

Additional information for patients is available on FDA's Heater-Cooler Devices "**Information for Patients (/MedicalDevices/ProductsandMedicalProcedures/CardiovascularDevices/Heater-CoolerDevices/ucm492585.htm)**" webpage.

As new and important information becomes available, the FDA will evaluate the information and update its recommendations, as appropriate.

FDA Activities

On December 29, 2015, the FDA issued a **Warning Letter (/ICECI/EnforcementActions/WarningLetters/2015/ucm479684.htm)** to Sorin Group Deutschland GmbH for its Stöckert 3T Heater-Cooler System after inspections conducted at facilities in Munchen, Germany and Arvada, Colorado revealed significant issues, including quality system and premarket clearance violations. Given the serious nature of the violations, the 3T devices manufactured by the Munchen facility are subject to import alert. This restricts the availability of the 3T devices to only those facilities that determine use of the device is medically necessary.

Sorin Group Deutschland GmbH initiated an ongoing corrective action for the 3T in July 2015, and has included updates to instructions for use with new cleaning instructions and instructions for determining if a device is contaminated with biofilm or NTM. Further updates to this recall are expected and will be evaluated by the FDA for their ability to further reduce infection risk. Please see the FDA medical device recall database entry for more information regarding corrective actions by the manufacturer:
http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfRES/res.cfm?start_search=1&knumber=K052601 (http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfRES/res.cfm?start_search=1&knumber=K052601)

EX. E

FDA continues to actively monitor this situation and will provide updates as appropriate.

Reporting Problems to the FDA

Device manufacturers and user facilities must comply with the applicable **Medical Device Reporting (MDR) regulations (/MedicalDevices/DeviceRegulationandGuidance/PostmarketRequirements/ReportingAdverseEvents/ucm200 05737.htm)**. Health care personnel employed by facilities that are subject to the **FDA's user facility reporting requirements (/MedicalDevices/DeviceRegulationandGuidance/PostmarketRequirements/ReportingAdverseEvents/ucm200 05737.htm)** should follow the reporting procedures established by their facilities.

Prompt reporting of adverse events can help the FDA identify and better understand the risks associated with the use of medical devices. Health care providers should submit voluntary reports of infection transmission associated with heater-cooler devices or reports describing difficulty following the manufacturers' instructions for use to the agency via the **Medical Device Reporting (MDR) (/MedicalDevices/Safety/ReportaProblem/ucm2005291.htm)** process. If a health care provider suspects bacterial contamination of the heater-cooler device following use, we encourage the health care provider to file a voluntary report through **MedWatch, the FDA Safety Information and Adverse Event Reporting program (/Safety/MedWatch/HowToReport/ucm2007306.htm)**.

Additional Resources

FDA Communications on Heater-Cooler Devices

Nontuberculous Mycobacterium Infections Associated with Heater-Cooler Devices: FDA Safety Communication (/MedicalDevices/Safety/AlertsandNotices/ucm466963.htm) (October 2015)

Heater-Cooler Informational Webpage (/MedicalDevices/ProductsandMedicalProcedures/CardiovascularDevices/Heater-CoolerDevices/ucm20082725.htm)

From the Centers for Disease Control and Prevention (CDC)

Interim Guide for the Identification of Possible Cases of Nontuberculous Mycobacterium Infections Associated with Exposure to Heater-Cooler Units (http://www.cdc.gov/hai/pdfs/outbreaks/Guide-for-Case-Finding.pdf) (May 2016)

Non-tuberculous Mycobacterium (NTM) Infections and Heater-Cooler Devices (http://www.cdc.gov/HAI/pdfs/outbreaks/CDC-Notice-Heater-Cooler-Units-final-clean.pdf) (October 2015)

Medical Literature

Sommerstein et al. 2016. Transmission of *Mycobacterium chimaera* from heater-cooler units during cardiac surgery despite an ultraclean air ventilation system. Emerging Infectious Diseases.

Garvey et al. 2016. Decontamination of heater-cooler units associated with contamination by atypical mycobacteria. J. Hospital Infection.

Contact Information

If you have questions about this communication, please contact the Division of Industry and Consumer Education (DICE) at **DICE@FDA.HHS.GOV (mailto:DICE@FDA.HHS.GOV)**, 800-638-2041 or 301-796-7100.

EX. E

[1] Haller S, Höller C, Jacobshagen A, Hamouda O, Abu Sin, M, Monnet, DL, Plachouras D, Eckmanns, T. 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. Euro Surveill. 2016;21(17):pii=3025. DOI: **http://dx.doi/10.2807/1560-7917.ES.2016.21.17.30215 (http://dx.doi/10.2807/1560-7917.ES.2016.21.17.30215)**

More in Safety Communications (/MedicalDevices/Safety/AlertsandNotices/default.htm)

2017 Safety Communications (/MedicalDevices/Safety/AlertsandNotices/ucm553873.htm)

2016 Safety Communications (/MedicalDevices/Safety/AlertsandNotices/ucm553855.htm)

EX. E

EX. E

EXHIBIT F
SORIN FIELD SAFETY NOTICE

SORIN GROUP
AT THE HEART OF MEDICAL TECHNOLOGY

SORIN GROUP DEUTSCHLAND GMBH Lindberghstr. 25 · D-80939 München

Customer Name
Address
City, State Zip

FIELD SAFETY NOTICE
Cardiac Surgery Mycobacterium Risks
Disinfection and Cleaning of Sorin Heater Cooler Devices

Affected Devices:	Sorin Group Perfusion System –Heater Cooler 3T devices (refer to Attachment 1 for affected catalog and serial numbers)
Date:	15 June 2015
Reference No:	9611109-06/03/15-002-C
Attention:	Hygiene Specialists, Cardiac Surgery Operating Room Responsible, Risk/Safety Managers, Distributors, Clinicians, Perfusionist and other users of these devices
Reason:	Sorin has become aware that the actual disinfection practices and the water maintenance that some users have been performing are not always conducted according to our Instructions for Use. Without vigilant performance of the disinfection and maintenance procedures per the Instructions for Use, organisms can multiply in a heater cooler device and potentially form biofilm. The biofilm provides an opportunity for bacteria, including Mycobacteria, to colonize within the device. Once colonized, there is a possibility that bacteria can become aerosolized when the heater cooler device is operated and serve as a source for contamination. Although water from the heater cooler device is not intended to contact the patient directly, fluid leakage from the device or aerosolization generated by a contaminated water circuit during device operation may create conditions in which the organisms could potentially contact the patient and subsequently contaminate the surgical site. Sorin Group is providing this notification to: (1) remind you of the importance of following the company's disinfection and maintenance procedures; (2) inform you that there is a possibility that bacteria can become aerosolized when the heater cooler device is operated and serve as a source for contamination; and (3) provide you with updated Instructions for Use regarding disinfection and maintenance procedures.

SORIN GROUP
DEUTSCHLAND GMBH
Lindberghstr. 25 · D-80939 München
T.: +49-(0)89-323 01 0
F.: +49-(0)89-323 01 100
www.sorin.com

Geschäftsführer:
Alexander H. J. Neumann
Giulio Cordano

Amtsgericht München
HRB 100852
USt-IdNr. (VAT) DE 129304291
Steuer-Nummer: 143/181/70429

EX. F

SORIN GROUP
AT THE HEART OF MEDICAL TECHNOLOGY

Dear Valued Customer:

The purpose of this letter is to advise you that Sorin Group Deutschland GmbH ("Sorin") is executing a voluntary field safety correction for the Heater Cooler 3T devices ("heater cooler devices"). This field safety notice describes below, immediate action to be taken by you.

- If your heater cooler device has been strictly maintained according to the Instructions for Use, please strictly adhere to the new Instructions for Use provided in **Attachment 1** of this letter.
- If your heater cooler device has **not** been strictly maintained according to the Instructions for Use, please perform the steps included in the *Immediate Customer Action* section of this letter.

Description of Issue

Sorin has become aware of cases of non-tuberculous mycobacteria endocarditis or deep infection following cardiac surgery during which the heater cooler device was used. There is a risk that surgical patients may experience invasive cardiovascular infection, including endocarditis, or other deep-surgical-site infections due to non-tuberculous mycobacteria, such as Mycobacterium chimaera. Because the symptoms may be slow to manifest, it is possible that many months may pass after completion of the surgical procedure before a surgical patient presents with an infection. In some cases, it is possible that infection could lead to death. Sorin's investigation into these cases is ongoing. To date, the investigation has not determined a causal connection between the heater cooler device and these cases. In some instances there has been a suggestion of such a link; however, infection following cardiac surgical procedures can be caused by numerous, other sources.

The heater cooler device which is provided non-sterile may develop highly contaminated water due to the failure to follow the Instructions for Use for water maintenance and water circuit disinfection. If contaminated water is used in the device **and** the user performs inadequate maintenance and/or fails to strictly adhere to the user instructions for cleaning of the heater cooler device, the device could become a source for contaminating the surgical environment. This condition can occur where there has been a build-up of biofilm within the water circuit of the device. Although water from the heater cooler device is not intended to contact the patient directly, fluid leakage from the device or aerosolization generated by a contaminated water circuit during device operation may create conditions in which the organisms could potentially contact the patient and subsequently contaminate the surgical site.

Contamination of heater cooler units with other waterborne pathogens, like *Mycobacterium abscessus* and non-fermenting gram-negative bacteria, has also been detected in the water of certain heater cooler units. However, no cases of patient infection have been determined to be caused by heater cooler devices. Further, Sorin's investigations into the potential association of heater cooler units with infections by *Mycobacterium chimaera* and other pathogens are ongoing.

If there is a need for further communication based on the investigation results, we will provide you the information.

SORIN GROUP
DEUTSCHLAND GMBH
Lindberghstr. 25 · D-80939 München
T.: +49-(0)89-323 01 0
F.: +49-(0)89-323 01 100
www.sorin.com

Geschäftsführer:
Alexander H. J. Neumann
Giulio Cordano

Amtsgericht München
HRB 100852
USt-IdNr. (VAT) DE 129304291
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EX. F

SORIN GROUP
AT THE HEART OF MEDICAL TECHNOLOGY

Immediate Customer Action

- ✓ Sorin reminds its customers using heater cooler devices about the importance of adhering to correct maintenance of the device at all times and, in particular, to assure that the cleanliness of the water is maintained. **Attachment 1** of this notification includes the new Instructions for Use for the cleaning and disinfection of the Sorin heater cooler devices. Please discard the existing IFU and follow this new IFU which includes updated cleaning and disinfection instructions.
    - o Assure that your team understands Mycobacteria and the potential contamination risks for cardiac surgical procedures, for example, that Mycobacterium is widely distributed in the ecosystem including chlorinated drinking water from the tap, it is inherently resistant to chemical disinfectants and antibiotics, and under the right conditions, it has a propensity to form biofilm and it can also be aerosolized.
- ✓ Healthcare providers involved in the care of patients who have undergone open heart surgery should be vigilant for cases of endocarditis or other cardiovascular infection of unidentified origin with specific testing for slow-growing non-tuberculous Mycobacteria such as *Mycobacterium chimaera* performed as indicated.
- ✓ Verify that this letter has reached your local team and that the recommended monitoring has been considered for your cardiac surgery operating rooms and area. This includes the monitoring of the area water not only for typical microorganisms, but also for slow growing non-tuberculosis Mycobacteria that requires special monitoring practices.

Actions to be taken by the user on the device

- ✓ Review your inventory and identify any heater cooler devices per the attached list, **Attachment 2**.
- ✓ For each unit, determine if the device has been maintained according to the Instructions for Use. If yes, strictly adhere to the new Instructions for Use provided in **Attachment 1** of this notification.

Note: It is recommended to implement a microbiological monitoring of the water quality (by heterotrophic plate count (HPC) measurement), including monitoring for non-tuberculous Mycobacteria on a monthly basis (Coliform bacteria, P. aeruginosa and non-tuberculous mycobacteria should not be detectable in 100ml). The water in the device should meet microbiological drinking-water quality according to national drinking-water standards.

SORIN GROUP
DEUTSCHLAND GMBH
Lindberghstr. 25 · D-80939 München
T.: +49-(0)89-323 01 0
F.: +49-(0)89-323 01 100
www.sorin.com

Geschäftsführer:
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EX. F

SORIN GROUP
AT THE HEART OF MEDICAL TECHNOLOGY

- ✓ If the device has not been maintained according to the Instructions for Use, follow instructions in the table below:
  Note: Please consult your Infection Control Manager for executing the following steps.

Step 1 / Submission of Test Sample
✓ Take two 100ml or greater water samples from one of the drain valves at the back of the device **prior to** the disinfection step: (1) for heterotrophic plate count measurement; and (2) for non-tuberculous mycobacteria analysis.
✓ Submit samples (1 & 2) to a microbiological lab for heterotrophic plate count measurement of the water and to determine if non-tuberculous mycobacteria are detectable.
✓ Perform disinfection of the water circuit of the heater cooler device(s) according to the new instructions for use provided in **Attachment 1** of this notification.
✓ Replace any accessories and products that are used in conjunction with the heater cooler device which may be potentially contaminated (e.g. tubing and connectors, graduated beaker, warming blanket) by new or re-processed parts.
✓ While awaiting test results from the microbiological lab, operate the heater cooler device outside of the operating room, if structurally possible, and proceed to **Step 2.** Note: For technical support regarding the installation outside the OR (max. distance, routing) please contact Technical Service Support at 1-800-221-7943 ext 6355
✓ If it is not possible to move the heater cooler device outside the operating room, take the device out of service or proceed to **Step 3.**
Step 2 / Interim Process (If heater cooler device can be operated outside the operating room)
✓ Perform the water maintenance and disinfection of the water circuit of the device(s) according to the new instructions for use provided in **Attachment 1** of this notification.
✓ Implement a bi-weekly microbiological monitoring of the water quality (by heterotrophic plate count (HPC) measurement), including monitoring for non-tuberculous mycobacteria. The samples shall be taken prior disinfection.
✓ When you receive the results from the lab go to **Step 4**

SORIN GROUP
DEUTSCHLAND GMBH
Lindberghstr. 25 · D-80939 München
T.: +49-(0)89-323 01 0
F.: +49-(0)89-323 01 100
www.sorin.com

Geschäftsführer:
Alexander H. J. Neumann
Giulio Cordano

Amtsgericht München
HRB 100852
USt-IdNr. (VAT) DE 129304291
Steuer-Nummer: 143/181/70429

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Step 3 / Heater Cooler operated in operating room
✓ Place the heater cooler in a way that the flow conditions of the surgical side are not disturbed by the heater cooler device fans. o Maintain maximum distance from surgical field; o Position heater cooler such that the fan exhausts of the device are directed away from the surgical field; o Position heater cooler fan exhausts close to the suction exhaust (outtake) of the operating room. ✓ The water in the tank must be changed **every day**. ✓ In order to prevent microbial growth and to avoid biofilm build-up, add medical grade 3% hydrogen peroxide solution to the tank contents (follow instructions provided in the new IFU, which direct 150 ml for the heater cooler 3T or 50 ml for the). ✓ Perform a **weekly** disinfection as described in the new IFU to kill the waterborne pathogens such as non-tuberculous mycobacteria. ✓ Implement a bi-weekly microbiological monitoring of the water quality (by heterotrophic plate count (HPC) measurement), including monitoring for non-tuberculous mycobacteria. The samples shall be taken prior to disinfection. ✓ Take microbiological air samples for non-tuberculous mycobacteria in the operating room when the heater cooler is running on a bi-weekly basis. ✓ When you receive the results from the lab go to **Step 4**
Step 4 / Review of Lab Analysis and Action
✓ If the microbial counts are within the specified limits (meet microbiological drinking-water quality and Coliform bacteria, P. aeruginosa and non-tuberculous mycobacteria are not detected in 100ml), the device can be placed back into the operating room. Continue to use and maintain the device according to the new IFU, **Attachment 1** ✓ Implement a microbiological monitoring of the water quality, including monitoring for non-tuberculous Mycobacteria on a monthly basis. ✓ If you find microbial counts in the water are greater than the limits specified above, immediately contact your infection control manager to determine appropriate actions ✓ If non-tuberculous mycobacteria are found in the air of the operating room, when the heater cooler is operated, remove the heater cooler from service. o For emergency surgeries please consult your infection control manager to determine appropriate actions.

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Geschäftsführer:
Alexander H. J. Neumann
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Amtsgericht München
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For technical support please contact the Technical Services hotline at 1-800-221-7943 X6355.

Please complete and return the attached Confirmation Form (see **Attachment 3**) by fax to 303-467-6502 or by email to yvonne.feyerherm@sorin.com.

Transmission of this Field Safety Notice

Please assure within your organization that this notice is communicated to all personnel who need to be aware of this Field Safety Notice. In case you have transferred products to a third party please communicate this information to them and also inform the below mentioned contact person.

Please maintain awareness on this notice and resulting action for an appropriate period to ensure effectiveness of the corrective action.

Contact reference person

For questions regarding this Field Safety Notice, please contact Amritt Khorran at 303-467-6306 or Yvonne Feyerherm at 303-467-6503 or by email to amritt.khorran@sorin.com or yvonne.feyerherm@sorin.com.

A copy of this Field Safety Notice has been provided to the appropriate Regulatory Agencies who are aware of these actions.

Thank you for your cooperation in this matter. Sorin Group is committed to provide quality products and service to its customers and we apologize for any inconvenience this situation may have caused.

Sincerely,

i.V. Christian Peis
Director Quality Assurance

Enclosures:

Attachment 1: New Instructions For Use

Attachment 2: Affected Product List

Attachment 3: Customer Response Form

SORIN GROUP
DEUTSCHLAND GMBH
Lindberghstr. 25 · D-80939 München
T.: +49-(0)89-323 01 0
F.: +49-(0)89-323 01 100
www.sorin.com

Geschäftsführer:
Alexander H. J. Neumann
Giulio Cordano

Amtsgericht München
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Attachment 2
Affected Product List

FIELD SAFETY NOTICE
Cardiac Surgery Mycobacterium Risks
Disinfection and Cleaning of Sorin Heater Cooler Devices
Reference # 9611109-06/03/15-002-C

Product Code	Product description	Affected Serial Number range
16-02-80	Heater-cooler 3T, 230V	16S10027 - 16S15641
16-02-81	Heater-cooler 3T, 240V	16S10743 - 16S11708
16-02-82	Heater-cooler 3T, 208V	16S10772 - 16S15523
16-02-83	Heater-cooler 3T, 127V	16S11455 - 16S15190
16-02-85	Heater-cooler 3T, 120V	16S10958 - 16S15634
16-02-95	Heater-cooler 3T, 200V	16S12004 - 16S15385

Please refer to Attachment 3 for affected Systems at your site.

SORIN GROUP
DEUTSCHLAND GMBH
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F.: +49-(0)89-323 01 100
www.sorin.com

Geschäftsführer:
Alexander H. J. Neumann
Giullo Cordano

Amtsgericht München
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Attachment 3 -
Customer Response Form

FIELD SAFETY NOTICE

Cardiac Surgery Mycobacterium Risks
Disinfection and Cleaning of Sorin Heater Cooler Devices
Reference # 9611109-06/03/15-002-C

According to our records you have the following affected products:

Product Code	Product description	Affected Serial Number

Please correct any inaccurate information above.

Please return this completed form to:
Yvonne Feyerherm by email: yvonne.feyerherm@sorin.com or by fax (303) 467-6502.

Section 1 - Please Complete:
We HAVE reviewed and understand the attached Field Safety Notice ☐ Yes ☐ No

We DO NOT understand the attached Field Safety Notice and request more information ☐ Yes ☐ No

WE HAVE discarded the old Instruction for Use ☐ Yes ☐ No

Customer Name: _____
Country: _____
Contact Name: _____
E-mail: _____
Fax No.: _____
Phone Number: _____

Submitted by .....
Signature ..... Date ...../...../.....

SORIN GROUP
DEUTSCHLAND GMBH
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www.sorin.com

Geschäftsführer:
Alexander H. J. Neumann
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EXHIBIT G
The July 15, 2015 Class 2 Recall Notice

Class 2 Device Recall STOCKERT HEATERCOOLER SYSTEM 3T

Class 2 Device Recall STOCKERT HEATERCOOLER SYSTEM 3T

See Related Information 22

Date Initiated by Firm	June 15, 2015
Date Posted	July 15, 2015
Recall Status[1]	Open[3], Classified
Recall Number	Z-2080-2015
Recall Event ID	71593[23]
510(K)Number	K052601[24]
Product Classification	Controller, temperature, cardiopulmonary bypass[25] - **Product Code** DWC[26]
Product	Sorin Stockert Heater-Cooler 3T, 120 V / 60 Hz Temperature control for extracorporeal perfusion of durations up to 6 hours.
Code Information	Product code 16-02-85 Serial number 16S10958-16S15634
Recalling Firm/ Manufacturer	Sorin Group USA, Inc. 14401 W 65th Way Arvada CO 80004-3503
For Additional Information Contact	Cheri Voorhees 303-467-6306
Manufacturer Reason for Recall	Potential colonization of organisms, including Mycobacteria, in Sorin Heater Cooler Devices, if proper disinfection and maintenance is not performed per Instructions for Use.
FDA Determined Cause [2]	Error in labeling
Action	Sorin Group issued a Field Safety Notice dated June 15, 2015, to all affected customers. The letter

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identified the product, the problem, and the action to be taken by the customer. Customers were instructed to review their inventory and identify any affected devices. For each unit customers were instructed to determine if the device has been maintained according to the Instructions for Use. If yes, customers should strictly adhere to the new Instructions for Use. Customers were also provide with a Response form to confirm they received, read and understood the Field Notice. Customers were instructed to return the completed form to assist in monitoring the effectiveness of the communication. For technical support customers should call 1-800-221-7943, ext 6355. For questions regarding this recall call 303-467-6306.

Quantity in Commerce 1755

Distribution Worldwide Distribution - US (nationwide) and Internationally to AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SK, AE, AR, AU, AZ, BD, BH, BR, BY, CA, CL, CN, CO, CR, DZ, EC, EG, ET, GE, GY, HK, ID, IL, IN, IQ, IR, JO, JP, KR, KW, KZ, LB, LK, LY, MA, MN, MU, MX, MY, NG, NP, NZ, OM, PA, PE, PH, PK, PR, PS, QA, RE, RU, SA, SG, SV, SY, TH, TN, TR, TT, TW, UA, VN, ZA.

Total Product Life Cycle TPLC Device Report[27]

[1] A record in this database is created when a firm initiates a correction or removal action. The record is updated if the FDA identifies a violation and classifies the action as a recall, and it is updated for a final time when the recall is terminated. Learn more about medical device recalls[28].

[2] Per FDA policy, recall cause determinations are subject to modification up to the point of termination of the recall.

[3] The manufacturer has initiated the recall and not all products have been corrected or removed. This record will be updated as the status changes.

510(K) Database 510(K)s with Product Code = DWC and Original Applicant = SORIN GROUP DEUTSCHLAND GMBH[29]

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20. /scripts/cdrh/cfdocs/cfClia/Search.cfm
21. /scripts/cdrh/cfdocs/cfTPLC/tplc.cfm
22. http://www.fda.gov/safety/recalls/enforcementreports/default.htm
23. /scripts/cdrh/cfdocs/cfRES/res.cfm?start_search=1&event_id=71593
24. /scripts/cdrh/cfdocs/cfpmn/pmn.cfm?ID=K052601
25. /scripts/cdrh/cfdocs/cfPCD/classification.cfm?ID=DWC
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27. /scripts/cdrh/cfdocs/cfTPLC/tplc.cfm?id=DWC
28. http://www.fda.gov/MedicalDevices/Safety/ListofRecalls/ucm329946.htm
29. /scripts/cdrh/cfdocs/cfPMN/pmn.cfm?start_search=1&productcode=DWC&knumber=&applicant=SORIN%20GROUP%20DEUTSCHLAND%20GMBH

Page Last Updated: 08/16/2017

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20. /scripts/cdrh/cfdocs/cfClia/Search.cfm
21. /scripts/cdrh/cfdocs/cfTPLC/tplc.cfm
22. http://www.fda.gov/safety/recalls/enforcementreports/default.htm
23. /scripts/cdrh/cfdocs/cfRES/res.cfm?start_search=1&event_id=71593
24. /scripts/cdrh/cfdocs/cfpmn/pmn.cfm?ID=K052601
25. /scripts/cdrh/cfdocs/cfPCD/classification.cfm?ID=DWC
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28. http://www.fda.gov/MedicalDevices/Safety/ListofRecalls/ucm329946.htm
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start_search=1&productcode=DWC&knumber=&applicant=SORIN%20GROUP%20DEUTSCHLAND%20GMBH

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EXHIBIT H
FDA October 15, 2015 Safety Communication

Nontuberculous Mycobacterium Infections Associated with Heater-Cooler Devices: FDA Safety Communication

Date Issued: October 15, 2015

Audiences:

- Health Care Providers who use heater-cooler devices
- Hospital staff who are responsible for operating and maintaining devices
- Infection Control Practitioners
- Infectious Disease Specialists
- Surgeons
- Perfusionists
- Operating Room Managers, Directors and Staff
- Risk Managers

Medical Specialties: Cardiothoracic Surgeons, Cardiovascular Surgeons, Orthopedic Surgeons, Neurosurgeons, General Surgeons, Anesthesiologists, Infection Control, Infectious Disease Physicians, Intensive Care Physicians

Product: All heater-cooler devices. Heater-cooler devices provide heated and/or cooled water to 1) oxygenator heat exchangers, 2) cardioplegia (paralysis of the heart) heat exchangers, and/or 3) warming/cooling blankets.

Purpose:
The FDA wants to heighten awareness about infections associated with heater-cooler devices and steps health care providers and health facilities can take to mitigate risks to patients.

Summary of Problem and Scope:
Heater-cooler devices are used during cardiothoracic surgeries, as well as other medical and surgical procedures to warm or cool a patient to optimize medical care and improve patient outcomes. Heater-cooler devices include water tanks that provide temperature-controlled water to external heat exchangers or warming/cooling blankets through closed circuits. Although the water in the circuits does not come into direct contact with the patient, there is the potential for contaminated water to enter other parts of the device or transmit bacteria through the air (aerosolize) through the device's exhaust vent into the environment and to the patient.

Through the FDA's analysis of adverse event reports, the medical literature, and information from national and international public health agencies, we are aware that the use of heater-cooler devices has been associated with Nontuberculous Mycobacteria (NTM) infections, primarily in patients undergoing cardiothoracic surgical procedures. NTM organisms are widespread in nature and can be found in soil and water, including tap water sources. They are typically not harmful, but in rare cases may cause infections in very ill patients and/or in individuals with compromised immune systems.

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Between January 2010 and August 2015, the FDA received 32 Medical Device Reports (MDRs) of patient infections associated with heater-cooler devices or bacterial heater-cooler device contamination. Twenty-five of these MDRs were reported to the FDA in 2015. Some reports describe NTM infections related to cardiothoracic surgeries, but other reports do not specify the procedure the patient was undergoing. Eight reports were related to 3 events describing patient infections occurring in U.S. health care facilities. The remaining 24 reports involved health care facilities outside the United States, most of these in Western Europe. In some cases, patients presented with infections several months to years after their surgical procedures. It is important to note that half of the 32 reports submitted to the FDA describe bacterial contamination of the heater-cooler device without known patient involvement or infection. The FDA is not aware of NTM infections acquired by hospital staff.

It is possible that some cases have not been reported to the FDA. It is challenging for a health care facility, health care provider, manufacturer, or patient to recognize that infections, particularly NTM infections, may be associated with the use of or exposure to a particular medical device. The FDA continues to evaluate reports through follow up with health care facilities and manufacturers to determine which factors may have contributed to the reported events.

Recommendations for Health Care Facilities and Staff
In addition to following standard precautions, the FDA recommends that facilities and staff using heater-cooler devices consider implementing the following measures to reduce risk to patients:

- Strictly adhere to the cleaning and disinfection instructions provided in the manufacturer's device labeling. Ensure you have the most current version of the manufacturers' instructions for use readily available to promote adherence.
- Do not use tap water to rinse, fill, refill or top-off water tanks since this may introduce NTM organisms. Use only sterile water or water that has been passed through a filter of less than or equal to 0.22 microns. When making ice needed for patient cooling during surgical procedures use only sterile water or water that has been passed through a filter of less than or equal to 0.22 microns. Deionized water and sterile water created through reverse osmosis is not recommended because it may promote corrosion of the metal components of the system.
- Direct the heater-cooler's vent exhaust away from the surgical field to mitigate the risk of aerosolizing heater-cooler tank water into the sterile field and exposing the patient.
- Establish regular cleaning, disinfection and maintenance schedules for heater-cooler devices according to the manufacturers' instructions to minimize the risk of bacterial growth and subsequent patient infection.
- Develop and follow a comprehensive quality control program for maintenance, cleaning, and disinfection of heater-cooler devices. Your program may include written procedures for monitoring adherence to the program and documenting set up, cleaning, and disinfection processes before and after use.
- Immediately remove from service heater-cooler devices that show discoloration or cloudiness in the fluid lines/circuits, which may indicate bacterial growth. Consult your hospital infection control officials to perform the appropriate follow up measures and report events of device contamination to the manufacturer.
- Consider performing environmental, air, and water sampling and monitoring if heater-cooler contamination is suspected. Environmental monitoring requires specialized expertise and equipment to collect and process samples, which may not be feasible in all facilities.
- Health care facilities should follow their internal procedures for notifying and culturing patients if they suspect infection associated with heater-cooler devices.
- Submit a report to the manufacturer and to the FDA **via MedWatch (/Safety/MedWatch/HowToReport/ucm2007306.htm)**, as described below, if you suspect heater-cooler devices have led to patient infections.

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FDA Activities:
The FDA is actively engaged with stakeholder groups to better understand the causes and risk factors for transmission of microbial agents associated with these devices and to develop strategies to minimize patient exposure. Our ongoing activities include:

- Working with health care facilities and professional medical societies to understand their experiences with heater-cooler devices.
- Evaluating information about documented and potential infections from multiple sources, including **medical device adverse event reports (/MedicalDevices/Safety/ReportaProblem/ucm2005291.htm)** submitted to the FDA, the medical literature, international public health agencies and federal partners.
- Collaborating with medical device manufacturers to review their existing cleaning and disinfection protocols provided in the instructions for use for currently marketed devices.

FDA continues to actively monitor this situation and will provide updates as appropriate.

Reporting Problems to the FDA:
Device manufacturers and user facilities must comply with the applicable **Medical Device Reporting (MDR) regulations (/MedicalDevices/DeviceRegulationandGuidance/PostmarketRequirements/ReportingAdverseEvents/ucm2005737.htm)**.

Health care personnel employed by facilities that are subject to the **FDA's user facility reporting requirements (/MedicalDevices/DeviceRegulationandGuidance/PostmarketRequirements/ReportingAdverseEvents/ucm2005737.htm)** should follow the reporting procedures established by their facilities.

Prompt reporting of adverse events can help the FDA identify and better understand the risks associated with the use of medical devices. Health care providers should submit voluntary reports of infection transmission associated with heater-cooler devices or reports describing difficulty following the manufacturers' instructions for use to the agency via the **Medical Device Reporting (MDR) (/MedicalDevices/Safety/ReportaProblem/ucm2005291.htm)** process. If a health care provider suspects bacterial contamination of the heater-cooler device following use, we encourage the health care provider to file a voluntary report through **MedWatch, the FDA Safety Information and Adverse Event Reporting program (/Safety/MedWatch/HowToReport/ucm2007306.htm)**.

Additional Resources:
Centers for Disease Control and Prevention. **Non-tuberculous Mycobacterium (NTM) Infections and Heater-Cooler Devices (http://www.cdc.gov/HAI/pdfs/outbreaks/CDC-Notice-Heater-Cooler-Units-final-clean.pdf)**. Safety Alert. October 2015.

American Thoracic Society. **An Official ATS/IDSA Statement: Diagnosis, Treatment and Prevention of Nontuberculous Mycobacterial Diseases: (https://www.thoracic.org/statements/resources/mtpi/nontuberculous-mycobacterial-diseases.pdf) (http://www.fda.gov/AboutFDA/AboutThisWebsite/WebsitePolicies/Disclaimers/default.htm)** 2007.

European Centre for Disease Prevention and Control (ECDC). **Rapid Risk Assessment: Invasive cardiovascular infection by *Mycobacterium chimaera* potentially associated with heater-cooler units used during cardiac surgery: (http://ecdc.europa.eu/en/publications/Publications/mycobacterium-chimaera-infection-associated-with-heater-cooler-units-rapid-risk-assessment-30-April-2015.pdf) (http://www.fda.gov/AboutFDA/AboutThisWebsite/WebsitePolicies/Disclaimers/default.htm)** April 30, 2015.

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References:

Kohler, P.; Kuster, SP.; Bloemberg, G. **Healthcare-associated prosthetic heart valve, aortic vascular graft, and disseminated *Mycobacterium chimaera* infections subsequent to open heart surgery. (http://eurheartj.oxfordjournals.org/content/ehj/early/2015/07/16/eurheartj.ehv342.full.pdf) (http://www.fda.gov/AboutFDA/AboutThisWebsite/WebsitePolicies/Disclaimers/default.htm)** Eur Heart J. 2015 Jul 17. *(Abstract)*

Sax, H.; Bloemberg, G.; Hasse, B.; et al. **Prolonged outbreak of *Mycobacterium chimaera* infection after open chest heart surgery. (http://cid.oxfordjournals.org/content/early/2015/03/11/cid.civ198.abstract) (http://www.fda.gov/AboutFDA/AboutThisWebsite/WebsitePolicies/Disclaimers/default.htm)** Clin Infect Dis. 2015 Mar 11. *(Abstract)*

Falkinham JO.; Pruden A.; Edwards M. **Opportunistic Premise Plumbing Pathogens: Increasingly Important Pathogens in Drinking Water. (http://www.mdpi.com/2076-0817/4/2/373/pdf) (http://www.fda.gov/AboutFDA/AboutThisWebsite/WebsitePolicies/Disclaimers/default.htm)** Pathogens 2015;4(2):373-386.

Contact Information:

If you have questions about this communication, please contact the Division of Industry and Consumer Education (DICE) at **DICE@FDA.HHS.GOV (mailto:DICE@FDA.HHS.GOV)**, 800-638-2041 or 301-796-7100.

More in Safety Communications (/MedicalDevices/Safety/AlertsandNotices/default.htm)

2017 Safety Communications (/MedicalDevices/Safety/AlertsandNotices/ucm553873.htm)

2016 Safety Communications (/MedicalDevices/Safety/AlertsandNotices/ucm553855.htm)

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EXHIBIT I
FDA Warning Letter

Sorin Group Deutschland GmbH 12/29/15

Department of Health and Human Services

Public Health Service
Food and Drug Administration
10903 New Hampshire Avenue
White Oak Building 66
Silver Spring, MD 20993

DEC 29, 2015

WARNING LETTER

VIA UNITED PARCEL SERVICE

André-Michel Ballester
Chief Executive Officer
LivaNova (formerly Sorin Group S.p.A.)
Via Benigono Crespi, 17
Milano, 20159
Italy

Dear Mr. Ballester**:**

The United States Food and Drug Administration (FDA) conducted the following inspections at your facilities:

- Sorin Group Deutschland GmbH, Lindberghstrasse 25, Munchen, 80939, Germany, (Munchen Facility), dated August 24, 2015, through August 27, 2015; and
- Sorin Group USA, Inc., 14401 W. 65th Way, Arvada, Colorado 80004, U.S.A., (Arvada Facility), dated August 24, 2015, through September 1, 2015.

During the inspection at your Munchen facility, investigators from the United States Food and Drug Administration (FDA) determined that your firm manufactures Stockert Heater Cooler 3T thermal regulator devices. Under section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act), 21 U.S.C. § 321(h), these products are devices because they are intended for use in the diagnosis of disease or other conditions or in the cure, mitigation, treatment, or prevention of disease, or to affect the structure or function of the body.

These inspections revealed that your firm’s devices are adulterated within the meaning of section 501(h) of the Act, 21 U.S.C. § 351(h), in that the methods used in, or the facilities or controls used for, their manufacture, packing, storage, or installation are not in conformity with the current good manufacturing practice requirements of the Quality System regulation found at Title 21, Code of Federal Regulations (CFR), Part 820.

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We received a response from Mr. Thierry Dupoux, Vice President, Sorin Group Cardiopulmonary BU, Sorin Group Deutschland GmbH, dated September 15, 2015, concerning our investigator's observations noted on the Form FDA 483s (FDA 483), List of Inspectional Observations, which was issued to your firm's Munchen, Germany facility. We address this response below, in relation to each of the noted violations. These violations include, but are not limited to, the following:

1. Failure to establish and maintain procedures for the identification, documentation, validation or where appropriate verification, review, and approval of design changes before their implementation, as required by 21 CFR 820.30(i) [Munchen Facility]. For example:

a. Your firm created Design Change Order #8115, dated December 11, 2012, as part of the corrective actions to the FDA Warning Letter dated August 2, 2011, to the Munchen Facility, to address deficiencies in the design change procedures. The change order documents the decisions to change the design input for water quality to add new cleanliness criteria, test the cleaning instructions for use (IFU) to the new input, update the cleaning instructions for use, and validate the new IFU. However:

i. The changed design input is incomplete in that there is no information on how maintaining a cleanliness standard for drinking water applies to the requirement that "biofilm should not grow in the 3T devices". Additionally, there is no information on a water quality standard ensures that the device does not cause waterborne infection; and,

ii. The design validation for the change to the cleaning IFU is inadequate. In the IFU, end users are responsible for conducting the cleaning and disinfection procedure on devices at user facilities. There is no documentation that your firm tested the updated IFU under actual or simulated use conditions to ensure the usability of the cleaning IFU. Your firm has received complaints of patient deaths due to infection from non-tuberculosis mycobacteria (NTM), specifically *mycobacteria chimaera,* since January 2014, where the cause of the infection appeared to be 3T devices colonized with the mycobacteria. Your firm investigated the complaints and determined that the user facilities had not been following the cleaning IFUs, potentially contributing to patient infections.

b. Your firm issued Design Change Orders 9416, 9416-01, 9711, and 9690, corresponding to CAPA 2015-03, and submitted a recall in June, 2015 (#Z-2076/2081-2015), to update the cleaning and disinfection IFU after receiving complaints of patient deaths due to infections caused by the 3T device. As part of this design change, your firm contracted a laboratory to conduct a test on the cleaning procedure in the updated IFU. The resulting test report, dated April 7, 2015, describes the test protocol and results. However, your firm's test report does not demonstrate an adequate verification or validation of the new cleaning IFU because: (reduction) for bacteria, as required by your test procedure. In addition the acceptance criteria do not appear to correspond to the design inputs of drinking water quality, controlling biofilm, or that the device does not cause waterborne infection;

i. The acceptance criteria for the test do not demonstrate that the updated cleaning and disinfection instructions produce a **(b)(4)** level (reduction) for bacteria, as required by your test procedure. In addition the acceptance criteria do not appear to correspond to the design inputs of drinking water quality, controlling biofilm, or that the device does not cause waterborne infection;

ii. Puristeril is not available in the United States, and therefore your firm recommends using Clorox as a substitute in the IFUs. However, the test report does not demonstrate the amounts of Clorox described in the IFU are equivalent to Puristeril;

iii. Two of the challenge bacteria, **(b)(4)** and **(b)(4),** used in the test procedure were not used at a high enough concentration to demonstrate the **(b)(4)** level acceptance criteria;

iv. The exact disinfectant dilution is not clear, because the exact water amounts used were not measured. Water levels were determined by **(b)(4).** No validation for the accuracy of these **(b)(4)** for detecting water levels was documented in the test report;

v. There is no description for how the sampling locations, sampling methods, and machine conditions used represent worst case condition for finding bacteria;

vi. There is no statistical rationale documented in the test report for using testing **(b)(4),** to demonstrate that the cleaning instructions for use will consistently maintain water quality requirements inside 3T devices in the field or clinical setting; and,

vii. There is no documentation that your firm tested the updated IFUs for usability by the end user. Specifically, those responsible for conducting the cleaning and disinfection procedure on devices at user facility.

Your firm's response did not address this deficiency. We note that this is a repeat from a nonconformance noted in the Warning Letter issued to the Munchen facility on August 2, 2011.

2. Failure to validate a process, with a high degree of assurance and approved according to established procedures, a process where results cannot be fully verified by subsequent inspection and test, as required by 21 CFR 820.75(a) [Munchen facility]. For example, your firm designed and implemented a new cleaning, drying, and disinfection process using **(b)(4)** at the contract manufacturer, **(b)(4),** as part of a corrective action. However, the new process was not adequately validated or verified prior to implementation on production units or monitored after implementation. Specifically:

a. Your firm contracted an "efficacy test" at a testing firm, **(b)(4)**, on November 17, 2014, to conduct an in-house validation of the use of the **(b)(4)** disinfection and drying process to eliminate a mycobacterium test strain from 3T devices to validate the new process. However, the efficacy test was not an adequate verification or validation of the disinfection and drying process because:

i. The efficacy test report documented testing to **(b)(4)** mixture**;** however, the disinfection and drying process **(b)(4).** There was no documentation of justification for using a different concentration, and therefore the test does not accurately reflect the **(b)(4)** disinfection procedure;

ii. No controls were used in the efficacy test;

iii. Your firm did not provide documentation to describe if a **(b)(4)** was used **(b)(4)**; and

iv. Your firm did not provide documentation for how the bacteria were **(b)(4).**

b. Your firm conducted further monitoring of manufactured devices after the **(b)(4)** disinfection and drying process was implemented. However, the monitoring was inadequate because the following required information for a cleaning and disinfection monitoring report was not documented:

i. The data for recovery efficiency of bacteria from the 3T devices;

ii. The data for complete bioburden: aerobic bacteria, anaerobic bacteria, spores, fungi, and yeast in the devices prior to disinfection. Only aerobic mesophilic bacteria are noted;

iii. The data for bacteriostasis or fungistasis;

iv. The concentration of **(b)(4)** used in sampling;

v. The time of exposure to the **(b)(4)**; and

vi. Whether **(b)(4)** was performed after **(b)(4).**

c. Your firm's disinfection and drying procedure and validation protocol, "**(b)(4)** cleaning, disinfection, and drying process designed and implemented by your Munchen facility at the contract manufacturer **(b)(4)**. However, the procedure was not adequately validated to ensure that the process completely dries the device.

For example:

i. The protocol states that the transparent pump tubing **(b)(4)** The protocol did not indicate whether any **(b)(4)** after drying was acceptable; and

ii. The validation did not include key technical parameters required for validation of a disinfection process. For example:

a. The amount of **(b)(4)** at time 0 (start of experiment);

b. Data to provide a rationale for choosing **(b)(4)** dry the tanks and tubing;

c. Quantification of the term "visually dry" and how to measure dryness by a validated method;

d. Documentation of the **(b)(4)**; and

e. Documentation of environmental conditions for temperature and humidity during the **(b)(4)** device prior to sampling.

We reviewed your firm's response and conclude that it is not adequate. Your firm did not evaluate the potential impact of these violations on distributed devices, and take steps to mitigate the risks as needed.

Our inspection also revealed that your firm's devices are misbranded under section 502(t)(2) of the Act, 21 U.S.C. § 352(t)(2), in that your firm failed or refused to furnish material or information respecting the device that is required by or under section 519 of the Act, 21 U.S.C. § 360i, and 21 CFR Part 803 - Medical Device Reporting (MDR), but are not limited to, the following:

3. Failure to adequately develop, implement, and maintain written MDR procedures, as required by 21 CFR 803.17 (Arvada facility). For example:

Your firm's MDR procedure, "Standard Operating Procedure for Medical Device Reporting", **(b)(4),** Rev. AA, updated on October 15, 2012, has the following deficiencies:

a. The procedure does not establish internal systems that provide for timely and effective identification, communication, and evaluation of events that may be subject to MDR requirements. For example, the procedure omits definition of the term "reasonably suggests," found in 803.20(c)(1). The exclusion of this definition for this term from the procedure may lead your firm to make an incorrect reportability decision when evaluating a complaint that may meet the criteria for reporting under 21 CFR 803.50(a);

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b. The procedure does not establish internal systems that provide for timely transmission of complete medical device reports. Specifically, the procedure does not address how your firm will submit all information reasonably known to it for each event;

c. The procedure does not describe how it will address documentation and record-keeping requirements, including:

i. Documentation of adverse event related information maintained as MDR event files'

ii. Information that was evaluated to determine if an event was reportable;

iii. Documentation of the deliberations and decision-making processes used to determine if a device-related death, serious injury, or malfunction was or was not reportable; and

iv. Systems that ensure access to information that facilitates timely follow-up and inspection by FDA.

In addition, we have noticed deficiencies in your firm's (Munchen facility) MDR procedure, **"(b)(4),** Rev. 003. Specifically, the MDR procedure does not have an effective date.

Please note, the MDR procedures at the Munchen and Arvada facilities include references to submitting MDRs to FDA using the following address: FDA, CDRH, Medical Device Reporting, P. O. Box 3002, Rockville, MD 20847-3002. Please note that effective August 14, 2015, MDRs should be submitted electronically and paper submissions will not be accepted, except under special circumstances, directed by FDA. For more information about electronic reporting, please refer to the eMDR website and the eMDR guidance document.
http://www.fda.gov/ForIndustry/FDAeSubmitter/ucm107903.htm (http://www.fda.gov/ForIndustry/FDAeSubmitter/ucm107903.htm)

Our inspection at your Munchen facility also revealed that the Heater Cooler 3T device is adulterated under section 501(f)(1)(B) of the Act, 21 U.S.C. § 351(f)(1)(B), because you do not have an approved application for premarket approval (PMA) in effect pursuant to section 515(a) of the Act, 21 U.S.C. § 360e(a), or an approved application for an investigational device exemption under section 520(g) of the Act, 21 U.S.C. § 360j(g). The Heater-Cooler System 3T is also misbranded under section 502(o) the Act, 21 U.S.C. § 352(o), because you did not notify the agency of your intent to introduce the device into commercial distribution as required by section 510(k) of the Act, 21 U.S.C. § 360(k).

Specifically, your firm distributed the Heater-Cooler System 3T, cleared under K052601, with modified Instructions for Use (Versions 013 and 014) with respect to the operating, maintaining, cleaning and disinfecting of the device. Some of the modifications found in Versions 013 and 014 include: adding more instruction details, changes to the cleaning/disinfecting process (e.g., chemicals used and amounts used), and expansion to the process to include the entire circuit instead of only the tanks. These are significant labeling changes that can affect the safety or effectiveness of the device, and therefore require a new 510(k) in order to be assured that appropriate testing and validation of the cleaning/disinfecting protocols have taken place.

For a device requiring premarket approval, the notification required by section 510(k) of the Act, 21 U.S.C. § 360(k), is deemed satisfied when a PMA is pending before the agency, 21 CFR 807.81(b). The kind of information you need to submit in order to obtain approval or clearance for the device is described on the Internet at:

http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/default.htm. (/MedicalDevices/default.htm)

The FDA will evaluate the information that you submit and decide whether your product may be legally marketed.

Our inspections also revealed that your firm's Heater-Cooler System 3T devices are misbranded under section 502(t)(2) of the Act, 21 U.S.C. § 352(t)(2), in that your firm failed or refused to furnish material or information respecting the device that is required by or under section 519 of the Act, 21 U.S.C. § 360i, and 21 CFR Part 806 – Medical Devices; Reports of Corrections and Removals. Significant violations include, but are not limited to, the following:

Failure to submit a written report to FDA of any correction or removal of a device initiated to remedy a violation of the act caused by the device which may present a risk to health, as required by 21 CFR 806.10. For example: A change order was initiated on December 20, 2011, related to a change consisting of updating the devices' IFU to indicate a new cleaning and disinfection procedure. Subsequently, the change was implemented in the IFU to indicate the use of a water filter and to add Hydrogen Peroxide to the water used in the devices. A letter was sent to your customers notifying them of the new IFU. The letter stated that the instructions for the device had been updated to assure the user can maintain the cleanliness of the water in the device, and that the 'Updated Instructions for Water Cleanliness' replaced the previous water cleaning instructions for the 3T Heater Cooler. Your firm did not submit a written report to FDA of the correction and removal, as required by 21 CFR 806.

Given the serious nature of the violations of the Act, the Heater Cooler 3T devices, and other devices manufactured by your Munchen facility are subject to refusal of admission under section 801(a) of the Act, 21 U.S.C. § 381(a), in that they appear to be adulterated. As a result, FDA is taking steps to refuse entry of these devices into the United States, known as "detention without physical examination," until these violations are corrected. In order to remove the devices from detention, your firm should provide a written response to this Warning Letter as described below and correct the violations described in this letter. We will notify you regarding the adequacy of your firm's response and the need to re-inspect your firm's facility to verify that the appropriate corrections and/or corrective actions have been made.

Also, U.S. federal agencies may be advised of the issuance of Warning Letters about devices so that they may take this information into account when considering the award of contracts. Additionally, premarket approval applications for Class III devices to which the Quality System regulation deviations are reasonably related will not be approved until the violations have been corrected.

Please notify this office, in writing within fifteen business days from the date you receive this letter, of the specific steps your firm has taken to correct the noted violations, including an explanation of how your firm plans to prevent these violations, or similar violations, from occurring again. Include documentation of the corrections and/or corrective actions (which must address systemic problems) that your firm has taken. If your firm's planned corrections and/or corrective actions will occur over time, please include a timetable for implementation of those activities. If corrections and/or corrective actions cannot be completed within fifteen business days, state the reason for the delay and the time within which these activities will be completed. Please provide a translation of documentation not in English to facilitate our review.

Your firm's response should be sent to: Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Field Inspections Support Branch, White Oak Building 66, Rm 2622, 10903 New Hampshire Ave., Silver Spring, MD 20993.Refer to CMS case #484629 when replying. If you have any questions about the contents of this letter, please contact: Shumaya Ali, Acting Chief, Foreign Enforcement Branch, at feb@fda.hhs.gov (email), or +1 (240) 402-4020 (phone), or +1 (301) 847-8139 (fax).

Finally, you should know that this letter is not intended to be an all-inclusive list of the violations at your firm's facility. It is your firm's responsibility to ensure compliance with applicable laws and regulations administered by

FDA. The specific violations noted in this letter and in the Inspectional Observations, FDA 483, issued at the close of the inspection may be symptomatic of serious problems in your firm's manufacturing and quality management systems. Your firm should investigate and determine the causes of the violations, and take prompt actions to correct the violations and bring the products into compliance.

Sincerely yours,
/S/
CAPT Sean Boyd
Acting Director
Office of Compliance
Center for Devices and
Radiological Health

Cc:
Thierry Dupoux
Vice President of Quality Assurance and Regulatory Affairs
LivaNova (formerly Sorin Group Deutschland GmbH)
Lindberghstrasse 25
Munchen, 80939
Germany

Carrie Wood
Director
Customer Quality
LivaNova (formerly Sorin Group USA)
14401 W 65th Way
Arvada, CO 80004

More in 2015 (/ICECI/EnforcementActions/WarningLetters/2015/default.htm)

EXHIBIT J
EuroSurveillance Article

Surveillance and outbreak report

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

S Haller [1], C Höller [2], A Jacobshagen [3], O Hamouda [1], M Abu Sin [1], DL Monnet [4], D Plachouras [4], T Eckmanns [1]
1. Department for Infectious Disease Epidemiology, Robert Koch Institute (RKI), Berlin, Germany
2. Bavarian Health and Food Safety Authority (LGL), Oberschleißheim, Germany
3. Federal Institute for Drugs and Medical Devices (BfArM), Bonn, Germany
4. European Centre for Disease Prevention and Control (ECDC), Stockholm, Sweden

Correspondence: Tim Eckmanns (eckmannst@rki.de)

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Invasive infections with *Mycobacterium chimaera* were reported in patients with previous open chest surgery and exposure to contaminated heater-cooler units (HCUs). We present results of the surveillance of clinical cases and of contaminated HCUs as well as environmental investigations in Germany up until February 2016. Clinical infections occurred in five male German cases over 50 years of age (range 53–80). Cases had been exposed to HCUs from one single manufacturer during open chest surgery up to five years prior to onset of symptoms. During environmental investigations, *M. chimaera* was detected in samples from used HCUs from three different countries and samples from new HCUs as well as in the environment at the manufacturing site of one manufacturer in Germany. Our investigation suggests that at least some of the *M. chimaera* infections may have been caused by contamination of HCUs at manufacturing site. We recommend that until sustainable measures for safe use of HCUs in operation theatres are implemented, users continue to adhere to instructions for use of HCUs and Field Safety Notices issued by the manufacturer, implement local monitoring for bacterial contamination and continuously check the websites of national and European authorities for current recommendations for the safe operation of HCUs.

Introduction

In July 2014, the Federal Office of Public Health Switzerland (FOPH) reported about patients with *Mycobacterium chimaera* infections, who had previously undergone open-chest heart surgery with exposure to contaminated heater-cooler units (HCUs) [1]. Several other reports and publications have suggested since that HCUs produced by one manufacturer in Germany may be a source of *M. chimaera* infections that occurred in Switzerland, Germany, the Netherlands and United Kingdom [2-5].

HCUs are commonly used in cardiac surgery during extracorporeal circulation in order to regulate the temperature of the blood and to provide temperature-controlled water for cardioplegia. HCUs have water tanks that provide temperature-controlled water to external heat exchangers. Since *M. chimaera* was detected in air samples close to operating HCUs, airborne transmission is believed to be the most likely transmission mechanism in the *M. chimaera* cases after open chest surgery [4,6].

M. chimaera is a slow-growing nontuberculous mycobacterium (NTM) belonging to the *M. avium* complex (MAC). It was first reported by Tortoli et al. in 2004 as a closely to *M. intracellulare*-related distinct species [7]. Identification requires molecular diagnostic testing [8]. *M. chimaera* may cause lung infections especially in patients with underlying lung disease as well as disseminated infections in immunocompromised patients and was found in skin and bone infections. In the environment, it was identified in biofilms and detected in water sources such as household water [9].

Among others, the report by the FOPH about the outbreak investigations in Switzerland and the reports about cases in Germany and the Netherlands led to increased surveillance efforts and outbreak investigations in Europe [3,10]. Here we present the results of the surveillance of clinical cases, of the surveillance of contaminated HCUs and of environmental investigations in Germany.

Table 1

Cases with symptomatic *Mycobacterium chimaera* infection, notified between April 2015 and February 2016, Germany (n=5)

Case number	Age (years)	Sex	Cardiac surgery centre	Type of surgery (exposure)	Prosthetic material	Site of infection	Death due to infection	Incubation period (years)[a]
1	80	Male	A	Aortic valve replacement	Yes	Endocarditis	No	<1
2	75	Male	B	CABG	No	Spondylodiscitis	No	5
3	65	Male	C	Aortic valve replacement	Yes	Valvular aortic endocarditis, paravalvular leak and abscess	Yes	3
4	67	Male	C	CABG and aortic valve replacement	Yes	Paravalvular abscess[c]	No[b]	4
5	53	Male	C	Aortic valve replacement	Yes	Endocarditis and cerebral abscesses	No	3

CABG: coronary artery bypass grafting.

[a] Time between exposure to open chest surgery involving use of an HCU and clinical diagnosis.

[b] Currently in palliative care.

[c] Endocarditis lenta and change of aortic valve in September 2013.

Methods

Definitions

For our investigations we used the following case definitions: a confirmed case was defined as a patient having undergone surgery with extracorporeal circulation in the five years before onset of symptoms of NTM infection AND in whom *M. chimaera* was detected in an invasive sample (e.g. blood, tissue biopsy or implanted prosthetic material). A probable case was defined as a confirmed case, but without detection of *M. chimaera* in an invasive sample.

An HCU was considered as contaminated, when cardiac surgery centres found NTM and/or other bacteria from environmental samples from the HCU and sent a report to the Federal Institute for Drugs and Medical Devices (BfArM) in Germany.

Prospective case finding and identification of contaminated HCUs

Prospective case finding was conducted from April 2015 onwards and results until end February 2016 are presented here. The mandatory surveillance of healthcare-associated outbreaks in Germany was applied for reporting clinical cases and this surveillance is described in detail elsewhere [11].

The public health authorities and healthcare professionals in Germany were informed about the ongoing outbreak and requested to notify cases fulfilling the case definition [12]. Specifically, the German National public health institute (Robert Koch Institute (RKI)), the German Society of Thoracic and Cardiovascular Surgery and the German Society of Infection informed federal states' authorities and societies' members, respectively, about case definitions and notification according to the article 6 of the 'Protection against Infection Act' (Infektionsschutzgesetz, IfSG) [12-15].

The mandatory notification system for incident reports of medical devices was used to detect contaminated HCUs in Germany. Incident reports were collected and analysed by BfArM in accordance with the corresponding legal framework 'The Act on Medical Devices' (Medizinproduktegesetz) and 'The Medical Device Safety Plan' (Medizinprodukte Sicherheitsplanverordnung).

HCU users were requested to submit any incident report associated with HCUs to BfArM [16]. On 10 July 2015, the BfArM recommended to place HCUs outside of the operation theatre and monitoring of contamination in HCUs [17].

At the European level, the European Centre for Disease Prevention and Control (ECDC) assessed the risk of invasive cardiovascular infection by *M. chimaera* potentially associated with heater-cooler units used during cardiac surgery in Europe also, in April 2015 [10]. The risk assessment was forwarded to regional German public health authorities. From April 2015 onwards, ECDC also provided a platform for exchange of information and a protocol for case detection and environmental testing [18]. The protocol was shared with all European Union/European Economic Area (EU/EEA) countries with the purpose to obtain information in a harmonised way, to further investigate the association between invasive infection by *M. chimaera* and HCUs, and to allow assessing the burden of these infections. The protocol was shared with the German heart surgery centres that detected clinical cases.

Table 2

Mycobacterium chimaera-positive samples from environmental investigations at the manufacturing site of new HCUs and of used HCUs from at the manufacturer's service centre, July 2014 to June 2015

Date	Type of sample	Source of sample
16 Jul 2014	Water (100 mL)	Used HCU from Switzerland
29 Jul 2014	Water (100 mL)	New HCU from manufacturing site
5 Aug 2014	Water (100 mL)	New HCU from manufacturing site
11 Aug 2014	Water (100 mL)	New HCU from manufacturing site
19 Feb 2015	Water (100 mL)	Used HCU from the Netherlands
10 Jun 2015	Water (volume not specified)	Sample taken in pump assembly area at the manufacturing site

HCU: heater-cooler unit.
The environmental investigations were performed by the manufacturer.

Investigation at the HCU manufacturing site and at the manufacturers' service centre

In July 2015, the Bavarian Health and Food Safety Authority (LGL), assisted the Bavarian regulatory authorities with on-site investigations and took environmental samples at the manufacturing site and in the service centre of the implicated manufacturer. Samples were taken from the production line, on-site tap water and from a used and disassembled HCU from this manufacturer in the service centre. All samples were sent to the National Reference Centre (NRC) for Mycobacteria Borstel, Germany.

On its own initiative, the HCU manufacturer conducted environmental sampling for NTM at the manufacturing site where the HCUs are assembled and in the service centre where used HCUs are disassembled for decontamination from July 2014 onwards. Environmental samples were sent to a local microbiological laboratory and NTM isolates were submitted to the NRC in Borstel for further analysis.

Culturing and typing

Mycobacteria were cultured in different laboratories. The development of standard protocols for microbiological *M. chimaera* diagnostic was coordinated by ECDC in collaboration with laboratories such as the NRC Borstel in Europe; these protocols were published by ECDC in August 2015 [18].

Next generation sequencing (NGS) of isolates is still ongoing.

Ethics

A formal ethical review process and approval was not required for this outbreak investigation in accordance with article 25, section 1 of the IfSG.

Results

At the beginning of our investigation, in April 2015, we were informed by cardiac surgery centre A in Germany about a confirmed case that became symptomatic before 2015 [3]. During April 2015 to February 2016, the mandatory surveillance of healthcare-associated outbreaks identified four additional confirmed cases of *M. chimaera* infection who had been exposed to an HCU in two different cardiac surgery centres (B and C) in Germany (Table 1). These cases developed a symptomatic *M. chimaera* infection five months to five years after exposure to a HCU. All five confirmed cases were male and aged above 50 years (range 53–80) when diagnosed with *M. chimaera* infection, four had aortic valve replacement and two underwent coronary artery bypass grafting, one died. All had been exposed to HCUs from one single manufacturer during open chest surgery. No cases with NTM infections other than *M. chimaera* were notified. Our investigations did not reveal epidemiological links between cases of the different sites.

Between January 2015 and February 2016, the BfArM received 26 incident reports of contaminated HCUs from 16 of the total of 78 German cardiac surgery centres from different German regions. Three of the 16 centres reported contamination of HCUs of another manufacturer but *M. chimaera* detection from these HCUs was not reported. Overall, the contaminations of the HCUs included *M. chimaera* and other bacteria such as *Pseudomonas aeruginosa*, *Legionella pneumophila* and *Stenotrophomonas maltophilia* and fungi. All three centres in which German cases were exposed sent incident reports about contamination of HCUs from the same German manufacturer. Two of these centres reported *M. chimaera* detection in HCU water samples including one reporting also detection of *M. chimaera* in air samples. The third centre reported NTM in HCU water samples, results of further specification were not reported.

During the environmental investigations performed by the Bavarian regulatory authorities on 2 July 2015, six of 20 samples obtained were *M. chimaera*-positive. All positive samples were from one disassembled HCU that had been used in cardiac surgery centre D in Germany and was disassembled for decontamination in the service centre of the manufacturer. The disassembled HCU was produced before modifications in the post-production process that were implemented

by the manufacturer in response to the findings of *M. chimaera* contamination. The samples included in the investigations were water (ca 100 mL), swab and biofilm and were collected from different sources: residual water, filler neck, patient bridge, biofilm from patient recirculation and patient bath.

In December 2015, the HCU manufacturer provided the RKI with information about six *M. chimaera*-positive samples from environmental investigations conducted between July 2014 and June 2015, including two contaminated HCUs from Switzerland and the Netherlands, respectively (Table 2).

On 22 December 2015, public health authorities in the EU/EEA and worldwide were notified by Germany about the suspected common source of *M. chimaera* via the EU Early Warning and Response System (EWRS) and via an International Health Regulation (IHR) notification.

Discussion

We present data that show that *M. chimaera* was isolated in clinical samples from (i) infected patients in Germany who had undergone open chest surgery, (ii) in samples from used HCUs from three different countries and (iii) in samples from new HCUs and the environment at the manufacturing site of one manufacturer. This suggests that at least some of the five German cases with *M. chimaera* infection may have occurred due to contamination of the HCUs by *M. chimaera* at the manufacturing site.

Preliminary typing results indicate that the *M. chimaera* isolates detected by the authorities and the isolates from the manufacturer appear to be almost identical (unpublished data). The *M. chimaera*-positive environmental samples at the manufacturing site prompted the manufacturer to modify the manufacturing process, which now includes ethanol disinfection and an active drying of the HCU water circuit before shipment. When the Bavarian regulatory authorities conducted onsite visits, no *M. chimaera*-positive sample was recovered except from a used HCU which had been disassembled for decontamination. The returned unit had been manufactured before August 2014. According to the information provided by the manufacturer, HCUs manufactured before mid-August 2014 may have had environmental mycobacteria presence in the unit at the time of delivery. Our investigations could not elucidate if and until when contaminated HCUs may have been delivered to customers from this manufacturer.

As of end of March 2016, two additional notifications of patients with *M. chimaera*-positive clinical specimens are under investigation in Germany. Until now we could not obtain data on all surgical interventions prior the *M. chimaera* diagnosis of these patients.

A limitation of our study is that we did not conduct active case finding. It is likely that the passive surveillance has led to an underestimation of the actual number of cases of *M. chimaera* infections in Germany. Furthermore, the true number of cases is probably underestimated since there is no typical clinical picture for infections with *M. chimaera*. Patients present with nonspecific symptoms, a variety of infection sites and a culture for mycobacteria is usually not part of a routine diagnostic work-up in patients presenting with signs of infection.

M. chimaera was not the only bacterial species isolated from HCUs. Contamination of HCUs with other bacteria was reported from various cardiac surgery centres in Germany. Furthermore, bacteria were also isolated from HCUs produced by other manufacturers. It is possible that some of the cases were infected due to contamination of HCUs at the cardiac surgery centres. It is also possible that some of the cases occurred due to exposure to HCUs produced by other manufacturers.

Infections by *M. chimaera* are rare and their occurrence, when detected, is considered unusual [19]. The reported *M. chimaera* infections might therefore be regarded as an indicator of a potential microbial hazard caused by the water-bearing HCUs in the healthcare environment.

Further investigations are needed to differentiate between the risk of *M. chimaera* infection from HCUs contaminated at the manufacturing site, the risk of infection from HCUs contaminated during use and the risk of infection from other medical devices that include an HCU such as extracorporeal membrane oxygenators [20]. In two recent publications, Götting et al. and Sommerstein et al. gave interesting insights into possible mechanisms of airborne transmission by HCUs [4,6]. In the cases described here, NGS should help determine the fraction that may be due to contamination at the manufacturing site or during use at the cardiac surgery centres.

To allow for targeted public health action, it is important that manufacturers of medical products share the findings of their own investigations into bacterial contamination, as demonstrated in this outbreak investigation. Sharing the results by the manufacturer, as well as information on the implemented corrective measures, allowed us to better understand the risks involved in HCU use. Regulatory authorities in Germany are continuing their information exchange with the manufacturers that produce HCUs to provide a sustainable solution for minimising the risks of infection in patients exposed to HCUs.

Conclusions

We present evidence on *M. chimaera* detection in clinical samples from infected German patients having been exposed to HCUs produced by the same manufacturer, in three cardiac surgery centres, in samples from used HCUs from three different countries and in samples from new HCUs and the environment at the manufacturing site of one manufacturer. In summary,

this suggests a point source for the reported *M. chimaera* infections and for *M. chimaera*-positive samples from HCUs and the environment. Notifications of contaminated HCUs of different manufacturers and with various bacteria, indicate a general problem with water-bearing systems in the healthcare environment.

We recommend that until sustainable measures for a safe use of HCUs in operation theatres are implemented, users continue to adhere to the instructions for use of the HCU and the Field Safety Notices issued by the manufacturer, implement a local monitoring for bacterial contamination of the HCUs and continuously check the websites of relevant national and European authorities for current recommendations for the safe operation of HCUs.

Acknowledgements

We would like to thank the HCU manufacturer for sharing their investigation results with the German authorities. The authors would like to thank colleagues of the NRC Borstel for the microbiological analysis. Furthermore, we would like to thank health personnel as well as local and regional public health authorities who notified clinical cases and contaminated HCUs. Finally we would like to thank HP Blank who supported surveillance and data management at RKI.

Conflict of interest

The authors have shared the manuscript with the manufacturer before publication. This has not led to changes of the content. The authors have declared that they have no competing interests.

Authors' contributions

SH, MAS, OH and TE were part of the outbreak team at RKI and conducted the epidemiological outbreak investigations. SH, TE and DP designed the investigation. SH, TE, DP, AJ, DLM and CH drafted the manuscript. All authors critically revised the manuscript and approved the final version. TE is corresponding author and guarantor.

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EXHIBIT K
July 2016 Adverse Event Report

MAUDE Adverse Event Report: SORIN GROUP DEUTSCHLAND SORIN HEATER-COOLER SYSTEM 3T CONTROLLER, TEMPERATURE, CARDIOPULMONARY BYPASS

SORIN GROUP DEUTSCHLAND SORIN HEATER-COOLER SYSTEM 3T CONTROLLER, TEMPERATURE, CARDIOPULMONARY BYPASS

Back to Search Results

Model Number 16-02-85
Device Problem Bacterial contamination of device
Event Date 04/04/2016
Event Type No Answer Provided
Manufacturer Narrative

Sorin implemented a field safety notice for disinfection and cleaning of sorin heater cooler devices. The z number is z-2076/2081-2015. Sorin group (b)(4) manufactures the sorin heater-cooler system 3t. The incident occurred in (b)(6). This medwatch report is being filed on behalf of sorin group (b)(4). Sorin group (b)(4) received a user medwatch report on (b)(4) 2016 stating that water samples were taken from the sorin heater-cooler system 3t unit per the (b)(4) advisory alert. The unit tested positive for mycobacteria intracellulare complex. There is no known patient involvement. Communication with the customer revealed that the unit is still in use at the facility, as there are no loaner units available. The facility reported that they have been following the cleaning instructions outlined in the instructions for use (ifu) since (b)(4) 2015. They did not state that the ifu was strictly followed before (b)(4) 2015. The investigation is ongoing. A follow-up report will be sent when the investigation is complete.

Event Description

Sorin group (b)(4) received a user medwatch report on (b)(6) 2016 stating that water samples were taken from the sorin heater-cooler system 3t unit per the pennsylvania advisory alert. The unit tested positive for mycobacteria intracellulare complex. There is no known patient involvement.

Search Alerts/Recalls[22]

New Search | Submit an Adverse Event Report[23]

Brand Name	SORIN HEATER-COOLER SYSTEM 3T
Type of Device	CONTROLLER, TEMPERATURE, CARDIOPULMONARY BYPASS
Manufacturer *(Section D)*	SORIN GROUP DEUTSCHLAND Lindberghstr. 25 Munich, 80939 GERMANY 80939
Manufacturer *(Section G)*	SORIN GROUP DEUTSCHLAND Lindbergstr. 25 Munich, 80939 GERMANY 80939
Manufacturer Contact	Carrie Wood 14401 W. 65th Way Arvada , CO 80004 3034676461
MDR Report Key	5774151
Report Number	9611109-2016-00392
Device Sequence Number	1
Product Code	DWC[24]
Report Source	Manufacturer
Source Type	HEALTH PROFESSIONAL

Reporter Occupation Health Professional
Remedial Action Notification
Type of Report Initial
Report Date 06/06/2016
***1* Device Was Involved in the Event**
***1* Patient Was Involved in the Event**
Date FDA Received 07/06/2016
Is This An Adverse Event Report? No
Is This A Product Problem Report? Yes
Device Operator Health Professional
Device MODEL Number 16-02-85
Was Device Available For Evaluation? No
Is The Reporter A Health Professional? Yes
Was the Report Sent to FDA?
Event Location No Information
Date Manufacturer Received 06/06/2016
Was Device Evaluated By Manufacturer? Device Not Returned To Manufacturer
Date Device Manufactured 06/23/2014
Is The Device Single Use? No
Is this a Reprocessed and Reused Single-Use Device? No
Type of Device Usage Reuse
Removal/Correction Number Z-2076/2081-2015

Patient TREATMENT DATA
Date Received: 07/06/2016 Patient Sequence Number: 1

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19. /scripts/cdrh/cfdocs/Medsun/searchReportText.cfm
20. /scripts/cdrh/cfdocs/cfClia/Search.cfm
21. /scripts/cdrh/cfdocs/cfTPLC/tplc.cfm

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22. https://www.fda.gov/MedicalDevices/Safety/ListofRecalls/default.htm
23. https://www.accessdata.fda.gov/scripts/medwatch/
24. ../cfPCD/classification.cfm?start_search=&ProductCode=DWC

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U.S. Food and Drug Administration
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Ph. 1-888-INFO-FDA (1-888-463-6332)
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17. /scripts/cdrh/cfdocs/cfPCD_RH/classification.cfm
18. /scripts/cdrh/cfdocs/cfAssem/assembler.cfm
19. /scripts/cdrh/cfdocs/Medsun/searchReportText.cfm
20. /scripts/cdrh/cfdocs/cfClia/Search.cfm

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21. /scripts/cdrh/cfdocs/cfTPLC/tplc.cfm
22. https://www.fda.gov/MedicalDevices/Safety/ListofRecalls/default.htm
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EXHIBIT L
CDC Health Advisory

Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

CDC Advises Hospitals to Alert Patients at Risk from Contaminated Heater-Cooler Devices Used during Cardiac Surgery

Distributed via the CDC Health Alert Network
October 13, 2016, 13:00 ET (1:00 PM ET)
CDCHAN-00397

Summary

The Centers for Disease Control and Prevention (CDC) is advising hospitals to notify patients who underwent open-heart (open-chest) surgery involving a Stöckert 3T heater-cooler that the device was potentially contaminated, possibly putting patients at risk for a life threatening infection. New information indicates that these devices, manufactured by LivaNova PLC (formerly Sorin Group Deutschland GmbH), were likely contaminated with the rare bacteria *Mycobacterium chimaera* during manufacturing. Hospitals should advise potentially exposed patients to seek medical care if they are experiencing symptoms such as night sweats, muscle aches, unexplained weight loss, fatigue, or unexplained fever. In addition, hospitals that use or have used this device are strongly encouraged to make and execute a plan to communicate with potentially exposed patients and to increase awareness among healthcare providers.

Background

In the spring of 2015, investigators in Switzerland reported a cluster of six patients with invasive infection of *M. chimaera*, a species of nontuberculous mycobacterium (NTM) commonly found in soil and water. The infected patients had undergone open-heart surgery that used contaminated heater-cooler devices during extracorporeal circulation (1). In July 2015, a Pennsylvania hospital also identified a cluster of invasive NTM infections among patients who had undergone open-heart surgery. CDC assisted in a field investigation that used both epidemiologic and laboratory evidence to identify an association between invasive *Mycobacterium avium* complex (including *M. chimaera*) infections and exposure to contaminated 3T heater-cooler devices, consistent with the Swiss report (2).

The water circuits in these heater-cooler devices that are used to regulate temperature during cardiopulmonary bypass do not come into direct contact with the patient's circulating blood; however, these reports suggest that *M. chimaera* can be aerosolized by the devices and result in infections (1,2). The Food and Drug Administration (FDA) and CDC have issued alerts about the need to follow updated manufacturer's instructions for maintenance and use of the devices, evaluate the devices for contamination, remain vigilant for new infections, and continue to monitor reports from the United States and overseas (2).

CDC in collaboration with National Jewish Health completed a whole-genome sequencing analysis and results demonstrate that *M. chimaera* isolates from patients with heater-cooler associated infections and from the 3T heater-cooler devices from several U.S. hospitals (in Pennsylvania and Iowa) are all highly related to each other (3). This evidence for likely point-source contamination of the 3T heater-cooler devices is consistent with recent reports from Europe (http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm504213.htm (http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm504213.htm)) that describe matching of *M. chimaera* sequences from environmental isolates at the device production site in Germany and isolates from patients and devices in Europe.

More than 250,000 heart bypass procedures using heater-cooler devices are performed in the United States every year; the 3T heater-cooler device linked to these infections represents about 60% of the heater-cooler devices in the country (2,4). In hospitals where at least one infection has been identified, the risk of infection was between about 1 in 100 and 1 in 1,000 patients. Initial information suggests that patients who had prosthetic material implanted are at

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highest risk for NTM infections. These infections are difficult to treat and delays in diagnosis further complicate patients' clinical management. Therefore, it is imperative that patients and providers are informed about the risk of infection associated with use of the 3T device and the need for appropriate diagnostic evaluation to facilitate timely diagnosis and treatment.

Recommendations

Healthcare providers

1. Internists, infectious disease specialists, cardiologists, cardiothoracic surgeons, and other clinicians should suspect NTM infections among patients who have signs of infection and a history of open-chest cardiac surgery.

- Infections can take months to cause symptoms.
- Patients with NTM infections following cardiac surgery have presented with a variety of clinical manifestations. Common examples are endocarditis, surgical site infection, or abscess and bacteremia. Other clinical manifestations have included hepatitis, renal insufficiency, splenomegaly, pancytopenia, and osteomyelitis.

2. Diagnosis can be difficult due to the nonspecific presentation of illness and the slow growing nature of the bacteria.

- Physicians should consider consulting with an infectious disease specialist if caring for patients who have undergone an open-chest cardiac procedure and present with signs of infection.
- Cultures for acid fact bacilli (AFB) should be obtained as part of the evaluation.
- Other specialized testing to detect *M. chimaera* may be needed and further laboratory testing should be discussed and arranged in consultation with an infectious disease specialist or health department.

Hospitals

1. Hospitals performing open-chest cardiac surgery should immediately assess their use of heater-cooler devices and determine whether they are currently using – or have previously used – 3T devices. Facilities should ensure that they are implementing current FDA recommendations to minimize patient risk to infections associated with heater-cooler devices (http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/UCM520191.htm (http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/UCM520191.htm%20)).
2. Hospitals should notify cardiothoracic surgeons, cardiologists, infectious disease physicians, internists, primary care physicians, and other clinicians who evaluate patients that have had open-chest cardiac or other bypass surgery, about the risk of infection associated with 3T heater-cooler devices. CDC has sample letters available at https://www.cdc.gov/hai/outbreaks/heater-cooler.html (https://www.cdc.gov/hai/outbreaks/heater-cooler.html).
3. Hospitals should review their facility's microbiology laboratory database and records of surgical procedures for any positive NTM cultures in surgery patients that might indicate a possible case. CDC has provided guidance on case-finding: http://www.cdc.gov/hai/pdfs/outbreaks/Guide-for-Case-Finding.pdf (http://www.cdc.gov/hai/pdfs/outbreaks/Guide-for-Case-Finding.pdf).
4. Hospitals should consider institution-specific strategies for alerting patients of the risk of infection related to potentially contaminated heater-cooler devices. CDC has sample patient notification letters available at https://www.cdc.gov/hai/outbreaks/heater-cooler.html (https://www.cdc.gov/hai/outbreaks/heater-cooler.html).
5. Hospitals can consider prospective surveillance of patients who have undergone open-chest cardiac surgery involving a 3T heater-cooler device.
6. Hospitals should consider using informed consent to educate patients of the potential NTM infection risk.
7. The overall risk of *M. chimaera* infection is low relative to other complications following cardiac surgery; emergent cardiac procedures should not be delayed because of the use of 3T devices. Continued use of 3T devices should be done in accordance with the latest manufacturer's recommendations, including maintenance and proper positioning of devices to minimize the risk of patient exposure.
8. Hospitals that have identified contaminated 3T heater-cooler devices or patient infections associated with devices should promptly alert their local or state health department and submit a report to FDA via MedWatch at http://www.fda.gov/Safety/MedWatch/HowToReport/DownloadForms/default.htm (http://www.fda.gov/Safety/MedWatch/HowToReport/DownloadForms/default.htm)

Health Departments

1. Health departments should communicate with healthcare facilities that perform cardiac surgery using heater-cooler devices about the risk of *M. chimaera* infection associated with open-chest cardiac surgery involving use of the 3T heater-cooler devices. Health departments should direct facilities to CDC and FDA heater-cooler guidance documents in these communications.

- CDC guidance documents can be found here:
  - http://www.cdc.gov/hai/pdfs/outbreaks/Guide-for-Case-Finding.pdf (http://www.cdc.gov/hai/pdfs/outbreaks/Guide-for-Case-Finding.pdf)
  - http://www.cdc.gov/HAI/pdfs/outbreaks/CDC-Notice-Heater-Cooler-Units-final-clean.pdf (http://www.cdc.gov/HAI/pdfs/outbreaks/CDC-Notice-Heater-Cooler-Units-final-clean.pdf)

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- FDA guidance documents can be found here:
  - http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm504213.htm (http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm504213.htm)
  - http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm466963.htm (http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm466963.htm)
  - http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/UCM520191.htm (http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/UCM520191.htm)

2. Health departments should track reports from healthcare facilities about potential infections associated with heater-cooler devices and encourage facilities to report these events to FDA.
3. Health departments should be prepared to assist healthcare facilities with further investigation; CDC is available for further consultation as needed.

Patients

1. Symptoms of NTM infection, including *M. chimaera* infection, can take months to appear. Patients should be aware of the symptoms of NTM infection which can include persistent or unexplained fever; night sweats; redness, heat, or pus around a surgical incision; muscle aches; unexplained weight loss; or fatigue.
2. Patients who have had cardiac surgery should seek medical evaluation if they have one or more of these symptoms or have questions about possible exposure to a heater-cooler device.

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The Centers for Disease Control and Prevention (CDC) protects people's health and safety by preventing and controlling diseases and injuries; enhances health decisions by providing credible information on critical health issues; and promotes healthy living through strong partnerships with local, national and international organizations.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

HAN Message Types

- **Health Alert:** Conveys the highest level of importance; warrants immediate action or attention. Example: HAN00001
- **Health Advisory:** Provides important information for a specific incident or situation; may not require immediate action. Example: HAN00346
- **Health Update:** Provides updated information regarding an incident or situation; unlikely to require immediate action. Example: HAN00342
- **Info Service:** Provides general information that is not necessarily considered to be of an emergent nature. Example: HAN00345

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This message was distributed to state and local health officers, state and local epidemiologists, state and local laboratory directors, public information officers, HAN coordinators, and clinician organizations.

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Additional Resources

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- HAN Types
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EXHIBIT M
FDA October 13, 2016
Updated Safety Communication

UPDATED: Mycobacterium chimaera Infections Associated with Sorin Group Deutschland GmbH Stöckert 3T Heater-Cooler System: FDA Safety Communication

The FDA is updating its June 1, 2016 **Safety Communication (/MedicalDevices/Safety/AlertsandNotices/ucm504213.htm)** to provide new information about *Mycobacterium chimaera* (*M. chimaera*) infections associated with the use of the 3T in U.S. patients who have undergone cardiothoracic surgeries. This communication also contains updated recommendations to help prevent the spread of infection related to the use of these devices.

October 13, 2016

Audiences:

- Health care providers who use 3T Heater-Cooler System
- Primary care providers who are responsible for the ongoing care of patients who have undergone cardiothoracic surgery
- Patients who have undergone cardiothoracic surgery
- Hospital staff who are responsible for operating and maintaining 3T Heater-Cooler System
- Health care facilities that perform procedures using the 3T Heater-Cooler System

Medical Specialties: Cardiothoracic Surgeons, Cardiovascular Surgeons, Orthopedic Surgeons, Neurosurgeons, General Surgeons, Anesthesiologists, Infection Control, Infectious Disease Physicians, Pediatrics, Primary Care, and Intensive Care Physicians

Product: The Stöckert 3T Heater-Cooler System (3T), manufactured by LivaNova PLC (formerly Sorin Group Deutschland GmbH) ,is intended to provide temperature-controlled water to 1) oxygenator heat exchangers, 2) cardioplegia (paralysis of the heart) heat exchangers, and/or 3) warming/cooling blankets to warm or cool a patient during cardiopulmonary bypass procedures lasting six hours or less.

Purpose: The FDA is updating its June 1, 2016 **Safety Communication (/MedicalDevices/Safety/AlertsandNotices/ucm504213.htm)** to provide new information about *Mycobacterium chimaera* (*M. chimaera*) infections associated with the use of the 3T in U.S. patients who have undergone cardiothoracic surgeries. This communication also contains updated recommendations to help prevent the spread of infection related to the use of these devices.

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As the FDA continues to investigate infections associated with the 3T, we believe health care facilities should take additional steps to help mitigate the risk of infection associated with the use of these devices

Summary of Problem and Scope:

Heater-cooler devices (http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/CardiovascularDevices/Heater-CoolerDevices/) are commonly used during cardiothoracic surgeries, as well as other medical and surgical procedures, to warm or cool a patient in order to optimize medical care and improve patient outcomes. Heater-cooler devices have water tanks that provide temperature-controlled water to external heat exchangers or warming/cooling blankets through closed circuits. Although the water in the circuits does not come into direct contact with the patient, there is the potential for contaminated water to enter other parts of the device and aerosolize, transmitting bacteria through the air and through the device's exhaust vent into the environment and to the patient. In October 2015, the FDA issued a **Safety Communication (/MedicalDevices/Safety/AlertsandNotices/ucm466963.htm)** to provide recommendations to help minimize patient risk of infections associated with heater-cooler devices. Since issuing that communication, the FDA has continued to evaluate the causes and risk factors for transmission of microbial agents associated with heater-cooler devices and has collaborated with professional societies, public health partners, and experts to develop strategies to minimize patient exposure.

A European study[1] published in April 2016 describes a link between *M. chimaera* clinical samples from several European infected cardiothoracic patients, samples from the heater-cooler devices used during these patient's procedures, and environmental samples from the device manufacturer's production and servicing facility in Germany. The results of this paper suggest a direct link between the *M. chimaera* that infected European patients during open-chest cardiac surgery, and the *M. chimaera* isolated from the 3T heater-cooler model utilized during these patients' surgeries.

M. chimaera is a type of nontuberculous mycobacterium (NTM) classified as a slow grower. *M. chimaera* may cause serious illness or death. The FDA believes *M. chimaera* infections associated with the 3T are rare. However, they are difficult to detect because infected patients may not develop symptoms or signs of infection for months to years after initial exposure.

On June 1, 2016, the FDA issued a **Safety Communication (/MedicalDevices/Safety/AlertsandNotices/ucm504213.htm)** specific to *M. chimaera* infections associated with the use of the 3T. Testing conducted by the manufacturer in August 2014 found *M. chimaera* contamination on the production line and water supply at the 3T manufacturing facility. The 3T devices manufactured at this facility were distributed worldwide. In response to the *M. chimaera* findings in August 2014, the manufacturer added cleaning and disinfection procedures to the production line in September 2014. Samples taken at the same manufacturing facility, by the German Regulatory Authorities in July 2015 did not show *M. chimaera*, potentially indicating the contamination at the manufacturing facility had been resolved. Although the manufacturer of 3T devices added cleaning and disinfection procedures to the production line in September 2014, the FDA is now aware of some 3T devices manufactured after September 2014 which have tested positive for *M. chimaera*. It has not been confirmed whether these devices were contaminated at the manufacturing facility or became contaminated at the user facility. To date, the FDA is not aware of *M. chimaera* patient infections associated with 3T devices that were manufactured after September 2014.

The June 1, 2016 **Safety Communication (/MedicalDevices/Safety/AlertsandNotices/ucm504213.htm)** also stated the FDA received reports of U.S. patients infected with *M. chimaera* after undergoing cardiothoracic surgery that involved use of the 3T devices. Each of

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those reports related to 3T devices that were manufactured prior to September 2014. The Centers for Disease Control and Prevention (CDC) in conjunction with National Jewish Health has **performed (https://www.cdc.gov/mmwr/volumes/65/wr/mm6540a6.htm?s_cid=mm6540a6_w)** whole genome sequencing on clinical isolates from infected patients and samples taken from the 3T devices from hospitals representing geographically distinct regions within the U.S. (Pennsylvania and Iowa) where clusters of patient infections with *M. chimaera* were identified. Each of the isolates tested were associated with devices manufactured before September 2014. Samples of the water drained from the 3T devices and air samples collected while the devices were in operation were also tested. The results obtained strongly suggest that the tested 3T devices had a common source of *M. chimaera* contamination. Sequence comparisons between U.S. and European Union (EU) samples, as well as samples from the manufacturing site, would provide additional information in evaluating the potential for point source contamination at the production site. However, EU sequencing results have not been shared to date.

As new information becomes available, the FDA will evaluate the information and update its recommendations, as appropriate.

UPDATED Recommendations for Health Care Facilities and Staff:

If your facility uses 3T devices, you should:

- **Immediately remove from service any heater-cooler devices, accessories, tubing, and connectors that have tested positive for *M. chimaera* or have been associated with known *M. chimaera* patient infections at your facility.**
- **Use new accessories, tubing, and connectors to prevent recontamination when using a different heater-cooler device.**
- **Direct and channel the heater-cooler exhaust away from the patient, e.g., to the operating room exhaust vent.**
- **Be aware that device contamination also may occur from other sources such as environmental contamination or device contact with contaminated accessories.**
- **Review the recommendations in CDC's Health Advisory (https://emergency.cdc.gov/han/han00397.asp)**
- **Be aware that heater-cooler devices are important in patient care. In appropriately selected patients, the benefits of temperature control during open chest cardiothoracic procedures generally outweigh the risk of infection transmission associated with the use of these devices.**

If your facility has 3T devices manufactured prior to September 2014, you should:

- **Strongly consider transitioning away from the use of these devices for open-chest cardiac surgery until the manufacturer has implemented strategies for these devices to mitigate the risks of patient infection.**
  - **Use of these devices should be limited to emergent and/or life-threatening situations if no other heater cooler devices are available.**
  - **Follow the FDA's earlier recommendations to help mitigate the risks of patient infection.**
  - **Be aware that testing of heater-cooler devices to identify units contaminated with *M. chimaera* presents technical challenges related to sample collection, the long culture time, and the high rate of false negative tests. Therefore, it is not recommended at this time.**

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If your facility has 3T devices manufactured after September 2014, you should:

- **Follow the FDA's earlier recommendations to help mitigate the risks of patient infection.**
- **Be aware that testing of heater-cooler devices to identify units contaminated with *M. chimaera* presents technical challenges related to sample collection, the long culture time, and the high rate of false negative tests. Therefore, it is not recommended at this time.**

The FDA recommends facilities and staff using heater-cooler units CONTINUE to implement the following measures to help reduce risk to patients:

- Strictly adhere to the cleaning and disinfection instructions provided in the manufacturer's device labeling. Ensure you have the most current version of the manufacturers' instructions for use readily available to promote adherence.
- Do not use tap water to rinse, fill, refill or top-off water tanks since this may introduce NTM organisms. Use only sterile water or water that has been passed through a filter of less than or equal to 0.22 microns. When making ice needed for patient cooling during surgical procedures use only sterile water or water that has been passed through a filter of less than or equal to 0.22 microns. Deionized water and sterile water created through reverse osmosis is not recommended because it may promote corrosion of the metal components of the system.
- Direct the heater-cooler's vent exhaust away from the surgical field to mitigate the risk of aerosolizing heater-cooler tank water into the sterile field and exposing the patient.
- Establish regular cleaning, disinfection and maintenance schedules for heater-cooler devices according to the manufacturers' instructions to minimize the risk of bacterial growth and subsequent patient infection.
- Develop and follow a comprehensive quality control program for maintenance, cleaning, and disinfection of heater-cooler devices. Your program may include written procedures for monitoring adherence to the program and documenting set up, cleaning, and disinfection processes before and after use.
- Immediately remove from service heater-cooler devices that show discoloration or cloudiness in the fluid lines/circuits, which may indicate bacterial growth. Consult your hospital infection control officials to perform the appropriate follow up measures and report events of device contamination to the manufacturer and to the FDA **via MedWatch (/Safety/MedWatch/HowToReport/ucm2007306.htm)**.
- Consider performing environmental, air, and water sampling and monitoring if heater-cooler contamination is suspected. Environmental monitoring requires specialized expertise and equipment to collect and process samples, which may not be feasible in all facilities.
- Health care facilities should follow their internal procedures for notifying and culturing patients if they suspect infection associated with heater-cooler devices.
- Submit a report to the manufacturer and to the FDA **via MedWatch (/Safety/MedWatch/HowToReport/ucm2007306.htm)**, if you suspect heater-cooler devices have been associated with patient infections.

Recommendations for Patients:

- Be aware that:
  - in the U.S., most cardiopulmonary bypass procedures involve the use of a heater-cooler device.

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- heater-cooler devices are important in patient care and, in appropriately selected patients, the benefits of temperature control necessary during open chest cardiothoracic proceduresgenerally outweigh the risk of infection transmission associated with using these devices.
- the FDA has received reports of patient infections associated with exposure to *M. chimaera* when contaminated 3T heater-cooler device were used during surgery.
- *M. chimaera* infections are difficult to detect because infected patients may not develop symptoms or signs of infection for months to years after initial exposure.
- there may be an increased risk of infection if you received a heart valve, graft, left ventricular assist device (LVAD), or any other prosthetic product/material or had a heart transplant.

- If you have undergone cardiopulmonary bypass, be aware of the possible signs and symptoms of NTM infection. These may include:
  - fatigue
  - fever
  - pain
  - redness, heat, or pus at the surgical site
  - muscle pain
  - joint pain
  - night sweats
  - weight loss
  - abdominal pain
  - nausea
  - vomiting
- If you have undergone a cardiopulmonary bypass procedure and are experiencing any of the signs and symptoms of NTM infection as outlined above, contact your health care provider as soon as possible.
- If you are not currently experiencing any changes in your general health, inform your health care provider during your next wellness visit that you have undergone a cardiopulmonary bypass procedure to determine if you require further testing or monitoring for possible exposure to NTM.

Additional information for patients is available on FDA's Heater-Cooler Devices "**Information for Patients (/MedicalDevices/ProductsandMedicalProcedures/CardiovascularDevices/Heater-CoolerDevices/ucm492585.htm)**" webpage.

FDA Activities:

On December 29, 2015, the FDA issued a **Warning Letter (/ICECI/EnforcementActions/WarningLetters/2015/ucm479684.htm)** to LivaNova PLC (formerly Sorin Group Deutschland GmbH) for its Stöckert 3T Heater-Cooler System after inspections conducted at facilities in Munchen, Germany and Arvada, Colorado revealed significant issues, including quality system and premarket clearance violations. Given the serious nature of the violations, the 3T devices manufactured by the Munchen facility are subject to import alert. This restricts the availability of the 3T devices to only those facilities that determine use of the device is medically necessary.

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Sorin Group Deutschland GmbH initiated an ongoing corrective action for the 3T in July 2015, and has included updates to instructions for use with new cleaning instructions and instructions for determining if a device is contaminated with biofilm or NTM. Further updates to this recall are expected and will be evaluated by the FDA for their ability to further reduce infection risk. Please see **the FDA medical device recall database entry (http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfRES/res.cfm?start_search=1&knumber=K052601)** for more information regarding corrective actions by the manufacturer.

In June 2016, the FDA **convened (/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/CirculatorySystemDevicesPanel/ucm485091.htm)** the Circulatory System Devices Panel of the Medical Devices Advisory Committee meeting and received expert clinical opinion and recommendations for patient notification and patient follow-up procedures. The panel also discussed **recommendations (/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/CirculatorySystemDevicesPanel/UCM505732.pdf)** for sampling and monitoring of the 3T and other heater-cooler devices, including regular visual monitoring of contamination within the water circuit, replacement of accessories (e.g. tubing) on a regular basis, and testing for water quality to assure adequate disinfection procedures are being performed. These recommendations are included in this Safety Communication.

The FDA continues to be actively engaged with the manufacturer, health care facilities and the CDC in evaluating risk and mitigation measures and will provide updates, as appropriate, as new information becomes available.

Reporting Problems to the FDA:

Device manufacturers and user facilities must comply with the applicable **Medical Device Reporting (MDR) regulations (/MedicalDevices/DeviceRegulationandGuidance/PostmarketRequirements/ReportingAdverseEvents/ucm2005737.htm)**. Health care personnel employed by facilities that are subject to the **FDA's user facility reporting requirements (/MedicalDevices/DeviceRegulationandGuidance/PostmarketRequirements/ReportingAdverseEvents/ucm2005737.htm)** should follow the reporting procedures established by their facilities.

Prompt reporting of adverse events can help the FDA identify and better understand the risks associated with the use of medical devices. Health care providers should submit voluntary reports of infection transmission associated with heater-cooler devices or reports describing difficulty following the manufacturers' instructions for use to the agency via the **Medical Device Reporting (MDR) (/MedicalDevices/Safety/ReportaProblem/ucm2005291.htm)** process. If a health care provider suspects bacterial contamination of the heater-cooler device following use, we encourage the health care provider to file a voluntary report through **MedWatch, the FDA Safety Information and Adverse Event Reporting program (/Safety/MedWatch/HowToReport/ucm2007306.htm)**.

Additional Resources:

- **FDA Communications on Heater-Cooler Devices**
  - **Mycobacterium chimaera Infections Associated with Sorin Group Deutschland GmbH Stöckert 3T Heater-Cooler System: FDA Safety Communication (/MedicalDevices/Safety/AlertsandNotices/ucm504213.htm)** (June 1, 2016) - ARCHIVED
  - **Nontuberculous Mycobacterium Infections Associated with Heater-Cooler Devices: FDA Safety Communication (/MedicalDevices/Safety/AlertsandNotices/ucm466963.htm)** (October 15, 2015)

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Heater-Cooler Informational Webpage (http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/CardiovascularDevices/Heater-CoolerDevices/default.htm)

- **From the Centers for Disease Control and Prevention (CDC)**
  - Perkins KM, Lawsin A, Hasan N, et al. ***Mycobacterium chimaera Contamination of Heater-Cooler Devices Used in Cardiac Surgery — United States (https://www.cdc.gov/mmwr/volumes/65/wr/mm6540a6.htm?s_cid=mm6540a6_w)***. MMWR Morb Mortal Wkly Rep 2016;65:1117–1118. DOI **https://emergency.cdc.gov/han/han00397.asp (https://emergency.cdc.gov/han/han00397.asp)**
  - **CDC Health Advisory: CDC Advises Hospitals to Alert Patients at Risk from Contaminated Heater-Cooler Devices Used during Cardiac Surgery (https://emergency.cdc.gov/han/han00397.asp)** (October 13, 2016)
  - **Interim Guide for the Identification of Possible Cases of Nontuberculous Mycobacterium Infections Associated with Exposure to Heater-Cooler Units (http://www.cdc.gov/hai/pdfs/outbreaks/Guide-for-Case-Finding.pdf)** (May 13, 2016)
  - **Non-tuberculous Mycobacterium (NTM) Infections and Heater-Cooler Devices (http://www.cdc.gov/HAI/pdfs/outbreaks/CDC-Notice-Heater-Cooler-Units-final-clean.pdf)** (October 27, 2015)
- **Medical Literature:**
  - Sommerstein et al. **Transmission of *Mycobacterium chimaera* from Heater-Cooler Units during Cardiac Surgery despite an Ultraclean Air Ventilation System.** Emerg Infect Dis. 2016 June;22(6):1008-13.
  - Garvey et al.**Decontamination of heater-cooler units associated with contamination by atypical mycobacteria**. J. Hospital Infection, Volume 93, Issue 3, July 2016:229-34.

Contact Information:

If you have questions about this communication, please contact the Division of Industry and Consumer Education (DICE) at **DICE@FDA.HHS.GOV (mailto:DICE@FDA.HHS.GOV)**, 800-638-2041 or 301-796-7100.

Haller S, Höller C, Jacobshagen A, Hamouda O, Abu Sin, M, Monnet, DL, Plachouras D, Eckmanns, T. 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. Euro Surveill. 2016;21(17):pii=3025. DOI: **http://dx.doi.org/10.2807/1560-7917.ES.2016.21.17.30215 (http://dx.doi.org/10.2807/1560-7917.ES.2016.21.17.30215)**

More in Safety Communications (/MedicalDevices/Safety/AlertsandNotices/default.htm)

Information About Heparin (/MedicalDevices/Safety/AlertsandNotices/ucm135345.htm)

Reducing Risks Associated with Medical Device Misconnections (/MedicalDevices/Safety/AlertsandNotices/TubingandLuerMisconnections/default.htm)

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