Infections associated with heater-cooler devices

Update

18 August 2017

Consumers and health professionals are advised that a total of six Australians have been confirmed with *Mycobacterium chimaera* infections following heart surgery involving heater-cooler devices.

NSW Health has reported four *Mycobacterium chimaera* patient infections, Victoria has reported one and the earliest case, in Queensland, is mentioned in our 2016 alert below. There have been no deaths reported.

Related information

- Non-tuberculous mycobacterium infections associated with heater-cooler devices
- Medical Devices Safety Update, Volume 4, Number 3, May 2016

As a result, the TGA has been conducting a product safety review into all heater-cooler devices supplied in Australia. Information about the progress of this review can be found in the table below.

The above confirmed cases of infection are associated with contaminated Stöckert Heater-Cooler 3T heater-cooler units that were manufactured before September 2014. See the section below - 'Contamination found in devices' - for more details.

Heater-cooler devices are used within operating theatres and intensive care units to control the temperature of blood during procedures where heating or cooling of blood is required. The devices contain water tanks that provide temperature-controlled water for the operation of the device. This water is not intended to come in contact with the patient or their blood.

The focus of the review is those heater-cooler devices intended to be used for cardiac bypass surgery

and extracorporeal membrane oxygenation (ECMO).

The TGA previously published advice (see below) regarding the potential for water within heater-cooler units to become contaminated with bacteria, most commonly non-tuberculous mycobacterium (NTM). There is evidence to suggest that patients are infected when bacteria in the device's water tank becomes airborne.

Approximately 100 patients worldwide have been identified as being infected with one species of NTM, *Mycobacterium chimaera*, following cardiac surgery. Cases of infection with *Mycobacterium chimaera* have been identified between three months and five years postoperatively.

An article published in The Lancet on 12 July 2017 provides further information about research that is being undertaken to determine the source of contamination and infection.

The risk of *Mycobacterium chimaera* infection in patients undergoing open-heart surgery has been estimated as 0.4-16 per 10,000 patient-years. 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%, the risk of infection by *Mycobacterium chimaera* is low.

TGA product safety review

The TGA safety review will investigate all heater-cooler devices included in the Australian Register of Therapeutic Goods (ARTG) that are characterised as containing water reservoirs that provide temperature-controlled water for the operation of the device and are used in cardiac procedures: bypass and ECMO.

The table below lists all of the medical devices included in the review that have been on the ARTG and are known to have been supplied in Australia. Some devices may no longer be used or are being used as back-up devices. This table is regularly updated.

Heater-cooler devices included in the TGA product safety review

Sponsor	Manufacturer	Australian Register of Therapeutic Goods number	Model / type of use	Regulatory and other action
Aurora BioScience Pty Ltd	Zoll Circulation	172677	Coolgard/ blood temperature control	• ARTG entry cancelled June 2011 • Review due to devices still in use, now complete.
Zoll Medical Australia Pty Ltd	Zoll Circulation	183013	Thermogard XP/blood temperature control	• Review completed. Minor amendments made to Instructions for Use which

				are approved as of 8 August 2017. • Disinfectant not required. This is a closed system that relies on a coolant fluid.
Australian Blood Management Unit Trust	Chalice Medical Ltd	238798	Paratherm/ECMO	• Suspension of the supply of this device was effective 21 April 2017. • A Safety Alert issued on 20 April 2017 provides information about an interim disinfection guide (pdf,122kb)for devices already in the market prior to the suspension (RC-2017-RN-00453-1).
Lovell Surgical Supplies International Pty Ltd	Medos Medizintechnik AG	262576	DeltaStream HC/ECMO	• A Recall for Product Correction: RC-2016-RN-00362-1 was issued on 7 April 2016 to update cleaning procedures. • Suspension of the supply of this device effective 2 June 2017 remains in place. • A Safety Alert (pdf,503kb) was issued on 7 July 2017 to provide an interim disinfection guide (pdf,242kb) for devices previously supplied (RC-2017-RN-00512-1).
LivaNova Australia Pty Ltd	Sorin Group Deutschland GmbH	194514	Flextherm/ bypass	• The TGA cancelled the Flextherm device from the ARTG, effective 4 July 2017.

				• The Flextherm device was discontinued and recalled on 14 March 2017 (RC-2017-RN-00252-1).
			Stockert Heater-Cooler 3T/bypass	• A Recall for Product Correction for the 3T device was issued on 16 June 2015 regarding the disinfection procedure (RC-2015-RN-00511-1). • A Recall for Product Correction for the 3T device was issued on 13 July 2016 (RC-2016-RN-00886-1) regarding the use of oxygenator mounting brackets. • A Safety Alert for IFU changes for the 3T device was issued in July 2016. The IFU advised on hydrogen peroxide use in the devices. • The 3T model is currently under review. The TGA is undertaking regulatory action under the Therapeutic Goods Act 1989
			Stockert Heater-Cooler 1T/bypass	• The TGA cancelled the Stockert Heater-Cooler 1T/bypass from the ARTG, effective 4 July 2017. • A Recall for Product Correction for the 1T device was issued on 16 June 2015 regarding the disinfection procedure (RC-2015-RN-00511-1). • A Safety Alert for IFU

				changes for 1T device was issued in July 2016. The IFU advised on hydrogen peroxide use in the devices.
Maquet Australia Pty Ltd	Maquet Cardiopulmonary AG	144010	HCU 20 Heater-Cooler/ bypass	• The TGA cancelled the device from the ARTG effective 25 July 2017.
			HCU 30 Heater-Cooler/ bypass	• The TGA cancelled the device from the ARTG effective 25 July 2017.
			HU 35 Heater Unit/ECMO	• Review completed. Instructions for Use updated and disinfectant indicated for use is now included on the ARTG. • Revised Instructions for Use approved as of 24 July 2017 (pdf,994kb)
			HCU 40 Heater-Cooler/ bypass	• Review completed. • Revised Instructions for Use approved as of 24 July 2017 (pdf,2.34mb) • Device remains included on the ARTG. IFUs updated and disinfectant indicated for use is now included on the ARTG.
Paragon Healthcare Pty Ltd	Cincinnati Sub Zero Products Inc	135587	Hemotherm CE 400/bypass	• The Hemotherm device is currently under review.

Contamination found in devices

The TGA has received reports for *Mycobacterium chimaera* contamination

How to access a pdf document

***Large file warning:** Attempting to open large

of three Stöckert 3T Heater-Cooler System (3T) devices manufactured after September 2014. The investigation into these recent reports is under way. The root cause has not yet been identified.

files over the Internet within the browser window may cause problems. It is strongly recommended you download this document to your own computer and open from there.

The TGA had previously received reports for *Mycobacterium chimaera* contamination of Stöckert 3T devices manufactured before September 2014, as reported in our previous web statement below. All patient infections have to date been associated with Stöckert 3T heater cooler devices manufactured prior to September 2014.

In addition, there have been two reports to date for NTM contamination in Maquet HCU 20 devices and one report of contamination in an HU 35 device supplied in Queensland. Two of the devices tested positive for *Mycobacterium chimaera* and have been decommissioned and one device was positive for *Mycobacterium gordonae*. This last device has been disinfected.

Unused units: There have been four reports to date of NTM contamination in unused ParaTherm Heater/Cooler units supplied to Queensland Health. In three of these cases *Mycobacterium chimaera* has been confirmed. In the other case the species of NTM involved is still to be confirmed.

ParaTherm Heater/Cooler units are not indicated for use in open-heart surgery, the surgical setting that is believed to pose the greatest risk of NTM infection.

There have been no incidents reported to the manufacturer, Chalice Medical Ltd, of NTM patient infection associated with the use of the ParaTherm Heater/Cooler.

The ParaTherm Heater/Cooler sponsor Australian Blood Unit Trust and manufacturer Chalice Medical Limited have advised the TGA that the cleaning protocol recommended in the product's Instructions for Use (IFU) is not successful at killing the NTM strain. The manufacturer is currently validating a more effective cleaning protocol and this will be introduced once relevant testing has been completed.

At this stage it is intended that the IFU will be updated via a recall for product correction and facilities will be notified once this occurs. In the meantime, the TGA has suspended this product from the ARTG. This means that no further units can be legally supplied, but existing units can continue to be used at the discretion of the health facility. The TGA is undertaking regulatory action under the *Therapeutic Goods Act 1989* to safeguard public health and safety.

Information for consumers and health professionals

Specific advice for consumers and health professionals regarding heater-cooler information, care and maintenance, and testing is detailed below.

Alert - updated advice for health professionals and facilities

28 October 2016

Consumers and health professionals are advised that the TGA has updated its information about mitigating the risk of *Mycobacterium chimaera* infections from heater-cooler devices. For more

details see 'Information for health professionals and facilities' below.

Heater-cooler devices are used within operating theatres to control the temperature of blood diverted to cardio-pulmonary bypass machines. Heater-cooler devices contain water tanks that provide temperature-controlled water for the operation of the device. This water does not come in contact with the patient.

The TGA published advice about this issue in a web statement on 2 August and in the May edition of *Medical Devices Safety Update.*

The Australian Commission on Safety and Quality in Health Care (ACSQHC) issued New National Infection Control Guidance relating to heater-cooler devices in September.

More than 50 patients worldwide have been identified with *Mycobacterium chimaera* infections after cardiac surgery. Cases of infection with *Mycobacterium chimaera* have been identified between three months and five years postoperatively. There is evidence to suggest that patients are infected when bacteria in the device's water bath becomes airborne.

There has been a single case report in Australia. The patient involved in this case is recovering.

Infection is a recognised consequence of all surgery and up to 3-5% of patients develop valve infections within the first 5 years after valve surgery. The risk for mycobacterial infection from contaminated aerosols from heater-cooler devices is considered to be very low compared with the overall risk of surgical and valve infection.

The US Food and Drug Administration issued a safety communication on 13 October in relation to contamination with *Mycobacterium chimaera* of one model of heater-cooler (Stöckert 3T Heater-Cooler System by LivaNova (Sorin)).

Based on the currently available data, and as determined by genomic sequencing of organisms, the *Mycobacterium chimaera* infections have been identified as a point source outbreak, with the heater-cooler units now believed to have been contaminated at the point of manufacture. The product affected is the Stöckert 3T Heater-Cooler System (3T) manufactured in Germany by LivaNova. The manufacturer implemented post-production/pre-shipping disinfection procedures on 18 August 2014 that have reduced the risk for units manufactured after September 2014.

Some sponsors of heater-cooler devices are undertaking recall actions in Australia (for example, updating the Instructions for Use regarding disinfection) to mitigate the risk of contamination. Recall actions are published in the System for Australian Recall Actions database.

TGA has received reports for *Mycobacteria chimaera* contamination of Stöckert 3T Heater-Cooler System (3T) devices.

Testing of Stöckert 3T Heater-Cooler System (3T) devices by hospitals in Australia has identified that 25% of these devices have tested positive for the Mycobacterium chimaera organism or other organisms. All devices that tested positive were manufactured prior to September 2014.

The overall issue of microbial contamination of heater-cooler-units was also highlighted in the United States when the University of Washington Medical Center reported contamination of three heater-cooler devices with *Legionella sp.* bacteria in September 2016. Four patients were diagnosed with

legionellosis (Legionnaires' disease) and two died. The source of the outbreak was linked to the hospital's water supply, as bacteria were also detected in an ice machine and two sinks in the hospital's cardiac unit. There have been no reports in Australia of heater-cooler devices being contaminated with *Legionella sp.* bacteria.

The TGA will continue to consult with an expert advisory panel regarding the issue of microbiological contamination of heater-cooler devices and to monitor the issue.

Information for consumers

Based on the currently available data, the risk of infection from contaminated aerosols from heater-cooler devices, in general, is thought to be very low.

If you, or somebody you provide care for, has undergone cardiac surgery in the previous 5 years, be aware of the possible signs and symptoms of *Mycobacterium chimaera* 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, or somebody you provide care for, is experiencing any of the signs and symptoms above following cardiac surgery, contact your doctor as soon as possible.

Information for health professionals and facilities

Consistent with the national guidance issued by the ACSQHC, the TGA recommends baseline testing, then follow-up testing in accordance with the manufacturer's instructions. Where information from the manufacturer is not available and the initial sample from the HCD is negative, then follow-up testing should occur at least every three months. This testing cycle should be maintained until further information about this situation becomes available.[1] The manufacturer's instructions will provide guidance on the type and frequency of testing with common elements being:

- Two microbiological methods are being recommended by some manufacturers - cultures of heterotropic plate counts (HPC) and mycobacterial cultures.
- Environmental samples should be submitted to a suitable laboratory identified in consultation

with the jurisdictional public health laboratory and tested using validated culture-based methods.

- Mycobacterial cultures of environmental samples requires specialised expertise, which may not be available in all facilities.
- Hospital protocols should account for the potential delay in receiving results from mycobacterial cultures, a clear result may take 6-8 weeks or longer.

If there are cases of legionellosis in patients, particularly cardiac surgery patients, then health professionals should consider the heater-cooler device as a possible source. Routine patient testing for legionellosis is not recommended at this time.

Addressing *Mycobacterium chimaera* infections

Reported infections overseas include surgical site infection, endocarditis, prosthetic valve infection, para-valvular abscess, graft infection and myocarditis. While initial case reports described mostly fatal infections, early recognition of *Mycobacterium chimaera* as the cause appears to result in better patient outcomes. Based on the available data, the case fatality rate is about 50%.

Some patients have presented with non-cardiac disease: granulomas, osteoarthritis, cholestatic hepatitis, nephritis, splenomegaly, or ocular disease.

Patients undergoing heart valve surgery, particularly with prosthetic implants, are considered to be at highest risk.

Based on the currently available data, the risk of infection from contaminated aerosols from heater-cooler devices, in general, is thought to be very low.

Heater-cooler devices are important in patient care and, in appropriately selected patients, the benefits of temperature control necessary during open chest cardiothoracic procedures outweigh the risk of infection transmission associated with using these devices.

Stratified risk mitigation for Stöckert 3T Heater-Cooler System (3T) devices

Risk mitigation advice for Stöckert 3T Heater-Cooler System (3T) devices manufactured before September 2014:

- Consider transitioning away from reliance on and the use of these devices (regardless of contamination status) 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 recommendations for all heater-cooler units (detailed below) to help mitigate the risks of patient infection.
    - Be aware that testing of heater-cooler devices to identify units contaminated with *Mycobacterium chimaera* presents technical challenges related to sample collection, the long culture time, and the possibility of false negative tests.

Risk mitigation for Stöckert 3T Heater-Cooler System (3T) devices manufactured after Sep 2014:

- Follow the recommendations for all heater-cooler units (detailed below) to help mitigate the risks of patient infection.

Risk mitigation for all heater-cooler units

- Strictly adhere to the cleaning and disinfection instructions provided in the manufacturer's device labelling. 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 non-tuberculous mycobacterium (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 aerosolising 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 minimise 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.
- Regularly check for and immediately remove from service heater-cooler devices and accessories that show discoloration of internal surfaces 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 TGA.
- Consider performing environmental (water) sampling of the water supply and monitoring if heater-cooler contamination is suspected. Environmental monitoring requires specialised expertise and equipment to collect and process samples, which may not be feasible in all facilities.
- Submit a report to the manufacturer and to the TGA, if you suspect heater-cooler devices have been associated with patient infections.

Patient 'look backs' following exposure

Currently, there are no evidence-based guidelines available on the follow-up of patients who have been exposed to a contaminated device.

Screening asymptomatic patients for NTM is currently not indicated. At this stage, the TGA recommends liaising with the medical director of the health facility and state/territory public health units to determine the most appropriate protocol in your jurisdiction.

Reporting problems

Consumers and health professionals are encouraged to report problems with medical devices. Your report will contribute to the TGA's monitoring of these products. For more information see the TGA Incident Reporting and Investigation Scheme (IRIS).

The TGA cannot give advice about an individual's medical condition. You are strongly encouraged to talk with a health professional if you are concerned about a possible adverse event associated with a medical device.

Footnote

1. New National Infection Control Guidance

Category: Alert/Advisory, Medical devices safety
Tags: surgical devices
URL: https://www.tga.gov.au/node/732320