# Welcome and Introduction

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June 2, 2016

# Public Health Concern

- **Nontuberculous mycobacteria (NTM) infections have been identified in patients who previously underwent cardiothoracic surgical procedures involving cardio-pulmonary bypass (CPB)**
- **Epidemiological investigations and lab analyses link these NTM infections with exposure to heater-cooler devices (HCDs) used during CPB**
- **HCDs are non patient contacting devices**
- **The airborne route for intraoperative transmission of NTM is newly described and was not anticipated when HCDs were previously cleared**

# Broad Approach

- **Multifaceted issue**
  - **Entire class of devices**
    - Device design and cleaning and disinfection methods
  - **Patient identification**
    - Patients may not manifest symptoms for months to years after initial exposure
    - Continuity of patient care
  - **Environmental factors**
    - Operating room environment
  - **Patient notification considerations**

# Meeting Discussion Topics

- **Effectiveness of HCD cleaning and disinfection methods**
- **Premarket data and information needed to demonstrate validation of cleaning and disinfection of HCDs to support labeling and technical instructions**
- **Protective measures and risk mitigations to ensure patient safety during procedures where these devices are used**
- **Developing risk stratification schema to inform guidelines for notifying patients who may have already been exposed to NTM during prior cardiac surgeries**

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**Overview of Heater-Cooler Devices**
**Nicole Milligan, BS**

HCD Validation: Cleaning and Disinfection
Elaine Mayhall, PhD

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# Overview of Heater Cooler Devices (HCD)

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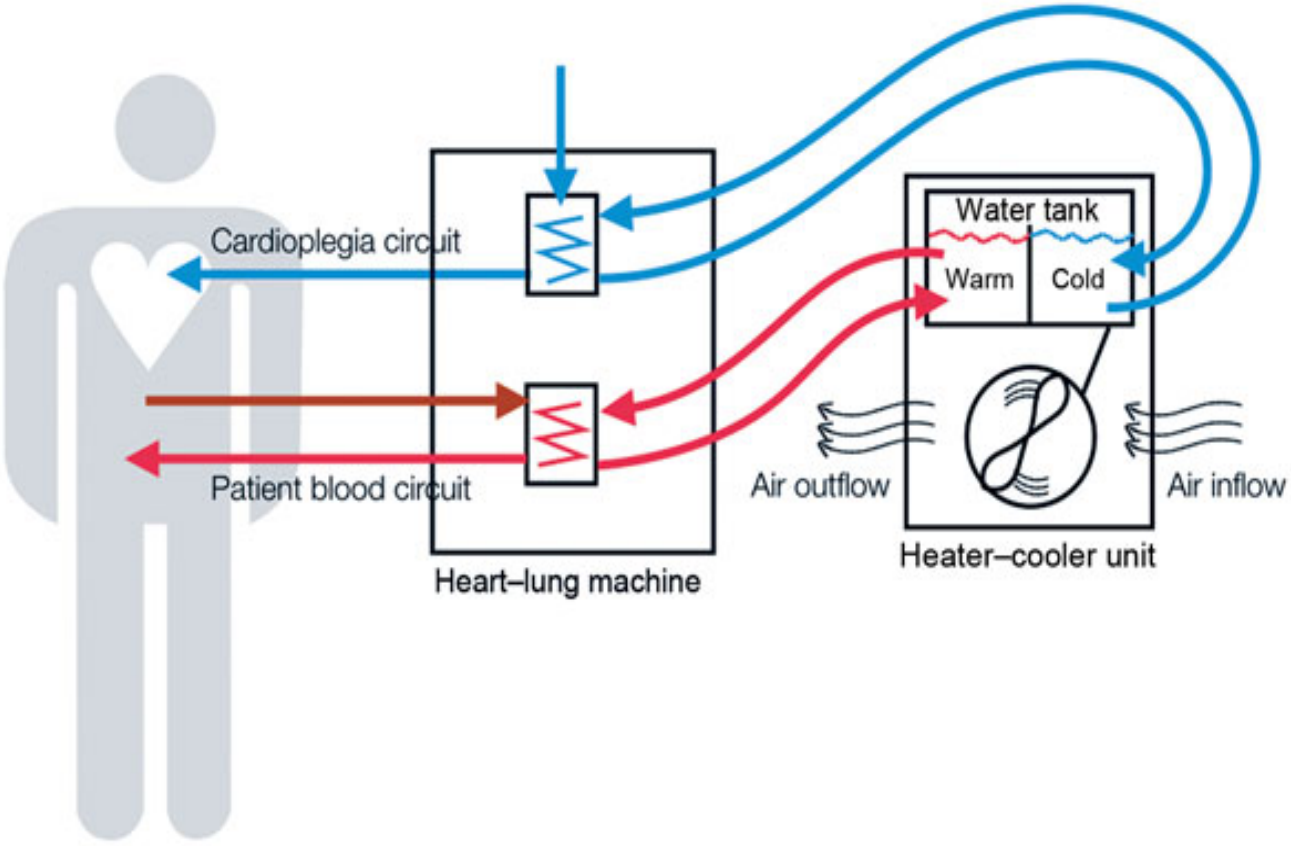
Office of Device Evaluation
Center for Devices and Radiological Health

# Overview

- **Background on HCDs**
- **Device Design**
- **Non-tuberculous Mycobacteria**
- **Challenges**

# General Description




Sommerstein R, Rüegg C, Kohler P, Bloemberg G, Kuster SP, Sax H. Transmission of *Mycobacterium chimaera* from heater-cooler units during cardiac surgery despite an ultraclean air ventilation system. Emerg Infect Dis. 2016 Jun

# 21 CFR 870.4250

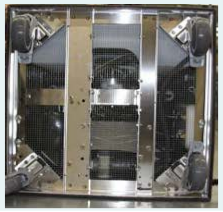
# Cardiopulmonary bypass temperature controller

## Identification

**A cardiopulmonary bypass temperature controller is a device used to control the temperature of the fluid entering and leaving a heat exchanger.**

# HCD Regulatory History

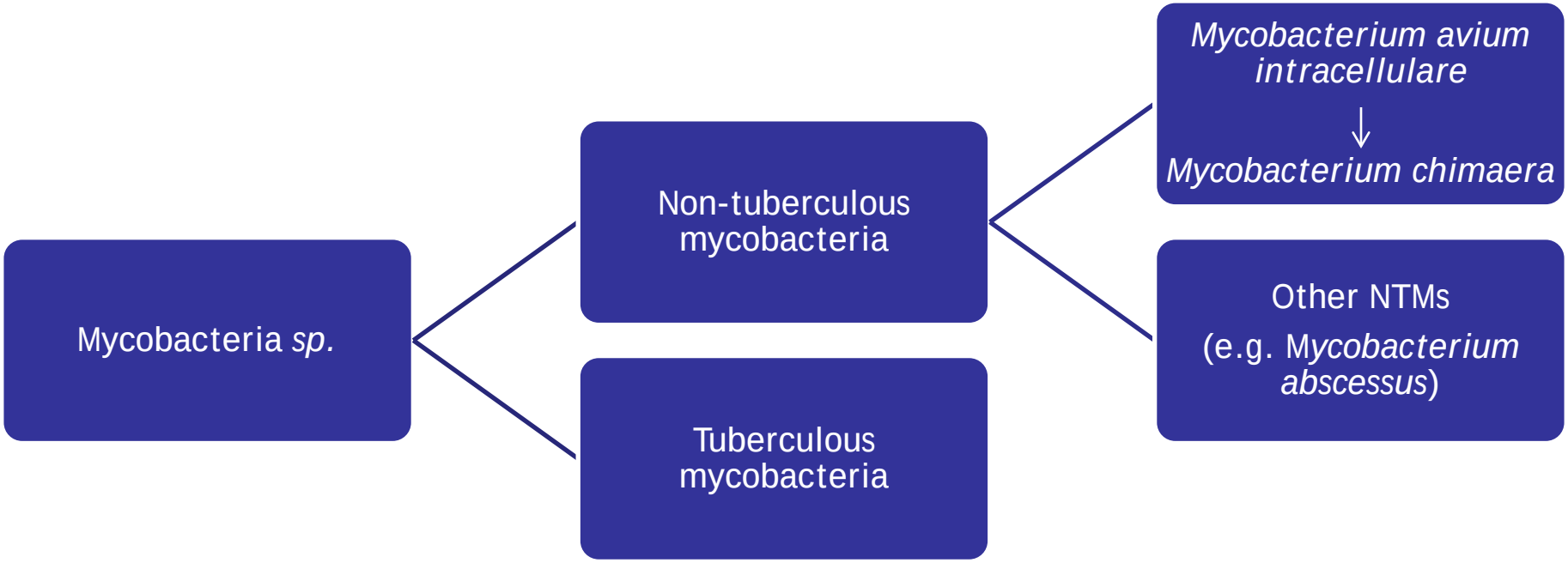
- **HCD's are Class II devices**
- **FDA regulatory review**
  - Performance
  - EMC
  - Software
  - Labeling (e.g., intended use)
- **Cleaning/Disinfection Procedures**
  - Water is not patient or blood contacting
  - Device is non-sterile
  - Risk to patient considered low
  - Quality Systems Regulation requires validated procedures

| Manufacturer | Model | Image |
|---|---|---|
| LivaNova/Sorin | Stockert 3T |   |
| Maquet | HCU 30 |   |
| Cardioquip | MCH 1000(i) |   |
| Terumo | TCM II |   |
| Cincinnati Sub Zero | Hemotherm 400CE |   |

# Design of HCDs

**All of the HCDs have design aspects that agitate the water and have fans with the potential to disrupt the laminar air flow in the OR.**

# What is Non-Tuberculous Mycobacteria (NTM)?



# NTM

- NTM wide spread in nature
- Isolated from natural water, tap water, soil, and water used in showers
- Surgical procedures (open chest) and more aggressive pathological profile than historically observed
- Spread likely through aerosolization

# Device Related Challenges

- **Water Tank and Other Circuit Component Access**
- **Connection to other circuit components**
- **Water Agitation within tanks**
- **Water/Air filters**
- **Fans/Vents**
- **Operating Temperature**
- **Future HCD Design Considerations**

*The committee will be asked to discuss device design features that could be improved for both current and future devices in order to mitigate aerosolization and minimize patient infection.*

# Device Related Challenges: Water Tank and Other Circuit Component Access

- **Some allow the end user access to the tank; others do not have practical access to the water tank.**
- **Tanks may have access but have coils which prevent adequate cleaning.**
- **Access to the HCD water tank and the ability to mechanically clean the tanks prior to disinfecting may be necessary to keep the tanks and circuits at an acceptable level of contamination.**

# Device Related Challenges: Connection to other circuit components

- **HCD is connected to several components (oxygenator/cardioplegia heat exchanger, blanket)**
- **These external devices may contain reusable components that are not part of the heater cooler device disinfection process**
- **Reconnection of a disinfected (or new) HCD to the contaminated external reusable components would readily contaminate the HCD**

# Device Related Challenges: Water Agitation within tanks

- **Agitation inside water tanks, created by mixing components, pumps, and the return water inlet, have the potential to produce air bubbles.**

- **These bubbles attract the hydrophobic NTM, and the amount of bubbles could influence the amount of aerosolized NTM within the tank.**

# Device Related Challenges: Water/Air filters

- **Water/Air filters with appropriate pore sizes should remove NTM from tap water and capture aerosolized NTM.**

- **Not all currently used HCDs contain water and air filters that would be suitable or practical for this need.**

# Device Related Challenges: Fans/Vents

- **Fans are found on all units and may facilitate the movement of aerosolized NTM**

- **Location of the vent and air exhaust may disturb airflow in the operating room**

# Device Related Challenges: HCD Operating Temperatures

**Operating temperatures of the HCD are well suited for NTM survival.**

# Device Related Challenges: Future HCD Design Considerations

- **Current HCD design features may contribute to biofilm formation and release of NTM into OR.**

- **New or modified HCD design features can be considered for reducing aerosolization.**

# Labeling Challenges

- **Water recommendations**
- **Cleaning/Disinfection Procedures**
- **Regular Maintenance/Servicing**

***The committee will be asked to comment on FDA's safety communication and provide other suggestions for devices on the market that may help mitigate or minimize patient infections from aerosolized NTM***

# Labeling Challenges: Water recommendations

- **Manufacturers' recommendations include tap water, distilled water, decalcified water, and filtered tap water.**
- **During disinfection, the tanks are rinsed with water prior to refilling for the next use.**
- **Sterile or filtered (with 0.22µm) water needs to be considered for filling (including ice making), re-filling, topping-off and cleaning/rinsing of the HCDs to limit NTM from being introduced into the circuit.**

# Labeling Challenges: Cleaning/Disinfection Procedures

- **Majority of HCDs recommend use of chemical agents to disinfect tank and circuits, while cleaning is conducted on the exterior of the device.**
- **In some cases, NTM is being found in HCDs, even after the recommended disinfection procedures have been followed.**
- **FDA recommends following the manufacturers' most current disinfection/cleaning instructions as deviations such as increased frequency could lead to degradation.**

# Labeling Challenges: Regular Maintenance / Servicing

- **HCDs need regular preventative maintenance at specified intervals to be performed by the manufacturer or trained representatives.**

- **Future servicing programs and/or manuals should prioritize their schedules/procedures to mitigate device contamination.**

# Point Source Contamination Challenges: Manufacturing Line

- **There may be one or many sources responsible for the introduction of NTM (e.g., tap water, ice machines, manufacturing line, etc.).**

- **The challenges with identifying source(s) include genotyping limitations, latency period, and traceability back to a specific HCD.**

# Environmental Challenges

- **Aerosolization of NTM within HCD and into OR**
- **Air flow in OR**
- **OR Infection Control Prevention**

# Environmental Challenges: Aerosolization of NTM within HCD and into OR

- **Tanks within the HCDs are not air or water sealed. Aerosolized NTM in the tanks may escape through unsealed openings into the casing of the HCD.**

- **Aerosolized NTM within the casing of the HCD can escape into the OR environment via vents, facilitated by fans.**

# Environmental Challenges: Air flow in OR

- **The HCD is placed outside the sterile field, and the patient is under a protective laminar flow of air.**

- **When the protection provided by the laminar flow is disrupted, particles already suspended in the OR air may settle inside the open wound during surgeries.**

# Environmental Challenges: OR Infection Control Prevention

**In the OR environment, proper air quality, air volume exchange, maintaining a positive pressure, proper air flow direction, and UV-C lighting may help reduce the transmission of airborne pathogens.**

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# HCD Validation: Cleaning and Disinfection

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# Water Quality Standards

- **EPA National Primary Drinking Water Regulations**
  40 CFR 141 National Primary Drinking Water Regulations
- **FDA-recognized Standard ANSI/AAMI 13959:2014 Water for hemodialysis and related therapies**

Note: Neither of these standards specify limits for NTM

*The committee will be asked to discuss whether or not one of these standards or another standard for microbial water quality can be used as a surrogate when determining acceptable levels of NTM in the HCD circulation water to minimize/mitigate patient infection.*

# Water Quality Standards

**EPA Primary Drinking Water Standard**

- ≤ 500 bacterial colonies/ml Heterotrophic plate count (HPC)

**ANSI/AAMI 13959:2014 Water for hemodialysis and related therapies**

- <1**00 cfu/ml** Total viable microbial counts in dialysis water
- Action level of **50 cfu/ml**.

# HCD Validation: Cleaning and Disinfection

**Manufacturer recommended cleaning and disinfection processes and frequencies have been ineffective in preventing contamination of HCDs with NTM and biofilm formation.**

*The panel will be requested to discuss how manufacturers should challenge the device in a lab environment that would replicate real-world use.*

# Disinfection of Medical Devices

| Device Type | Patient Contact | Disinfection/ Sterilization |
|---|---|---|
| Semi-critical | Mucous membranes or non-intact skin | Sterilization but high level disinfection is acceptable |
| Non-critical Instruments | Intact skin | Low or intermediate level disinfection |
| Non-critical Equipment surfaces | Indirect | Low level disinfection |
| | | |
| HCD | No intended patient contact | Panel advice requested |

# Disinfection Endpoints

- **High level disinfection:**
  - 6-log ($10^6$) reduction of a mixed suspension of vegetative organisms, such as *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Escherichia coli*, and representatives of the Klebsiella-Enterobacter group, and
  - 6-log ($10^6$) reduction of an appropriate mycobacterium species
- **Intermediate level disinfection:**
  - 6-log ($10^6$) reduction of the mixed suspension of vegetative organisms, such as *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Escherichia coli*, and representatives of the *Klebsiella*-Enterobacter group, and
  - 3-log ($10^3$) reduction of an appropriate mycobacterium species

# HCD Disinfection Validation Testing

- **Potency testing of disinfectants**
- **Simulated use testing**
- **In use testing**

# Potency Testing

- **EPA Registered antimicrobial/disinfectant**
- **Potency testing**
  - Tuberculocidal Activity
  - Fungicidal Activity
  - Bactericidal Activity
  - Virucidal Activity

# Simulated Use Testing

- **Test devices –** Use of conditioned devices
- **Organic challenge** – Simulate actual use conditions
- **Test organisms -** Relevant waterborne test organisms, *Pseudomonas aeruginosa* and nontuberculous mycobacterium (NTM), for example, *Mycobacterium abscessus*, *M. fortuitum*, *M. mucogenicum*, *M. avium*, *M. chimaera*
- **Inoculation** – At most difficult areas of the device for disinfectant to penetrate

# Simulated Use Testing

- **Challenge quantification –** Before and after disinfection cycle
- **Recovery and Culturing**
  - Water samples
  - Internal surfaces, including biofilm
- **Treatment**

# Proposed HCD Disinfection Endpoints - Simulated Use Testing

- 3-log ($10^3$) kill of an appropriate NTM (*M. abscesses, M. fortuitum,* or *M. mucogenicum*) species, and

  6-log ($10^6$) kill of the vegetative bacteria (*P. aeruginosa*, etc.)

**OR**

- 6-log **($10^6$)** kill of an appropriate NTM (*M. abscesses, M. fortuitum,* or *M. mucogenicum*) species, and

  6-log ($10^6$) kill (microbicidal) of the vegetative bacteria (*P. aeruginosa*, etc.)

# Simulated Use Testing

*The panel will be asked to discuss how manufacturer's should develop validated disinfection processes that properly challenge HCDs in a laboratory environment that would replicate real-world use and what endpoints would be appropriate to apply in simulated use testing for disinfection of HCD water pathways to demonstrate that acceptable levels of NTM in HCD circulation water are achieved and maintained.*

# In Use Testing

- Clinical setting
- Cleaning and disinfection process per label instructions and carried out by healthcare personnel
- Evaluate over extended period of time
- Worst case conditions for HCD use including periods of inactivity
- Water samples collected and tested for microbial levels
- Internal surface swab samples collected and tested for microbial load; presence of biofilm

# Decontamination of heater-cooler units

**"Decontamination of heater-cooler units associated with contamination by atypical mycobacteria"**

- **MI Garvey, R Ashford, CW Bradley, CR Bradley, TA Martin, J Walker, and P Jumaa**
- **Journal of Hospital Infection, In Press**

Three different HCD decontamination regimens were evaluated for reducing the total viable count (TVC) from >300 cfu/100 ml in the water of HCDs.

# Garvey et al.

| Regimen | Disinfectant | TVC Disinfection | TVC Weekly |
|---|---|---|---|
| 1- Manufacturer's | Chlorine-based | >300 cfu/100 ml | >300 cfu/100 ml* |
| 2- 2X | Chlorine-based | 1 cfu/100 ml | 1-300 cfu/100 ml* |
| 3- 2x | Peracetic acid | 0 cfu/100 ml | 1-100 cfu/100 ml |
| 4 – Regime 3 plus tubing change | Peracetic acid | 0 cfu/100 ml | 0 cfu/100 ml |

***** M. chimaera found

**Conclusion:** A decontamination cycle, including an initial replacement of internal tubing with weekly microbiological water samples is required to maintain the water quality within HCDs at an acceptable level.

# Question to Panel

*The committee will be asked to discuss whether monitoring or surveillance of the HCD water for NTM or bacterial contamination should be performed to determine that the water quality within the HCD is maintained at an acceptable level.*

# Other Bench Testing

**Compatibility of disinfectant and disinfection process with HCD**

- Material compatibility
- Device functionality
- Device specifications

# Challenges

NTM are difficult to identify and the slow growing varieties require long grow-out times. Standards exist that set limits for microbial water quality, but do not specify limits for NTM.

- Can a standard that specifies microbial water quality be used as a surrogate when determining acceptable levels of NTM in the HCD water to minimize NTM growth and biofilm formation?
- Should the HCD water be monitored for NTM or bacterial contamination in the clinical setting?

# Challenges (cont.)

HCDs have no intended patient contact but NTM found in HCD water can be aerosolized and ultimately transmitted into the OR environment to infect a patient's chest wound. However, these devices do not fit into the scheme used for determining the appropriate disinfection level.

- How should a manufacturer challenge the HCD to replicate real-world use and validate the disinfection process?
- What endpoints for disinfection should be used in simulated use testing to demonstrate the effectiveness of the cleaning/disinfection instructions?

# HCD Validation: Cleaning and Disinfection

**Thank you**

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# Multi-pronged FDA Investigative Process

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June 2, 2016

# Multi-pronged FDA Investigative Process

- Outreach
- Compliance
- Communications
- Medical Device Report Analysis
- Information Request Letters

# Outreach

- **Ongoing collaboration with:**
  - CDC Division of Healthcare Quality Promotion
  - States: Health Departments, Association of State/Territorial Health (ASTHO)
  - International Public Health Agencies: England, Ireland, Germany, Netherlands, Switzerland, Denmark, etc.
  - Experts: Joseph Falkinham Ph.D, Richard Wallace M.D., Hugo Sax M.D., Andrew Streifel M.S., Silvia Muñoz-Price M.D. Ph.D
  - Professional Societies: Society for Healthcare Epidemiology of America (SHEA), Infectious Disease Society of America (IDSA)
  - Veteran's Administration

# Activities

- **Hospital Outreach**
  - Extensive follow-up with hospitals about Medical Device Reports
  - Hospital visits
  - Medical Product Safety Network (MedSun) survey
- **CDC convened Healthcare Infection Control Practices Advisory Committee (HICPAC) presentation**
- **50 states call**
  - Heighten State awareness of NTM infections in cardiothoracic patients
  - Inform stakeholders of ongoing and upcoming FDA & CDC efforts
  - Provide recommendations and resources to aid in risk reduction

# Compliance: Inspections and Actions

- Directed inspections at heater-cooler device manufacturers are under way
- Several inspections have been completed and resulted in actions including a Warning Letter and Import Alert
- Focus for inspections is ensuring that firms have strong quality system and reporting procedures in place

# FDA Communications

## Safety Communication 10/15/15

http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm466963.htm

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Medical Devices

Home › Medical Devices › Medical Device Safety › Safety Communications

Safety Communications

- Information About Heparin
- Preventing Tubing and Luer Misconnections

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

SHARE | TWEET | LINKEDIN | PIN IT | EMAIL | PRINT

**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

## Webpage 3/28/16

http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/CardiovascularDevices/Heater-CoolerDevices/default.htm

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Heater-Cooler Devices

- Concerns about Nontuberculous Mycobacteria Infections Associated with Heater-Cooler Devices
- Information for Health Care Providers
- Information for Patients
- FDA's Ongoing Investigation of Nontuberculous Mycobacteria Infections Associated with Heater-Cooler Devices
- Additional FDA Activities and Collaborative Efforts
- Additional Resources
- Reporting Problems to the FDA

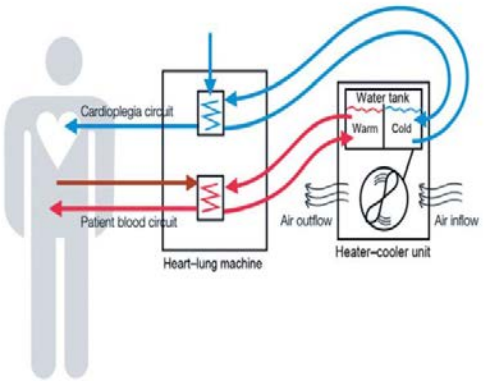
Resources for You

- Federal Register: Circulatory System Devices Panel of the Medical Devices Advisory Committee; Notice of Meeting; Establishment of a Public Docket; Request for Comments

### Heater-Cooler Devices

SHARE | TWEET | LINKEDIN | PIN IT | EMAIL | PRINT

Heater-cooler devices are often necessary for use during surgeries to warm or cool patients as part of their care. They are especially important tools for surgeries involving the heart, lungs, esophagus, and other chest organs (cardiothoracic surgeries). Heater-cooler devices, as shown below in Figure 1[1], include tanks that provide temperature-controlled water to external heat exchangers or to warming/cooling blankets through closed water circuits.



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# Medical Device Report (MDR) Review

## Heater-Cooler MDRs Associated with Infection/Contamination

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**Nurse Consultant**

**Division of Postmarket Surveillance**

**Office of Surveillance and Biometrics**

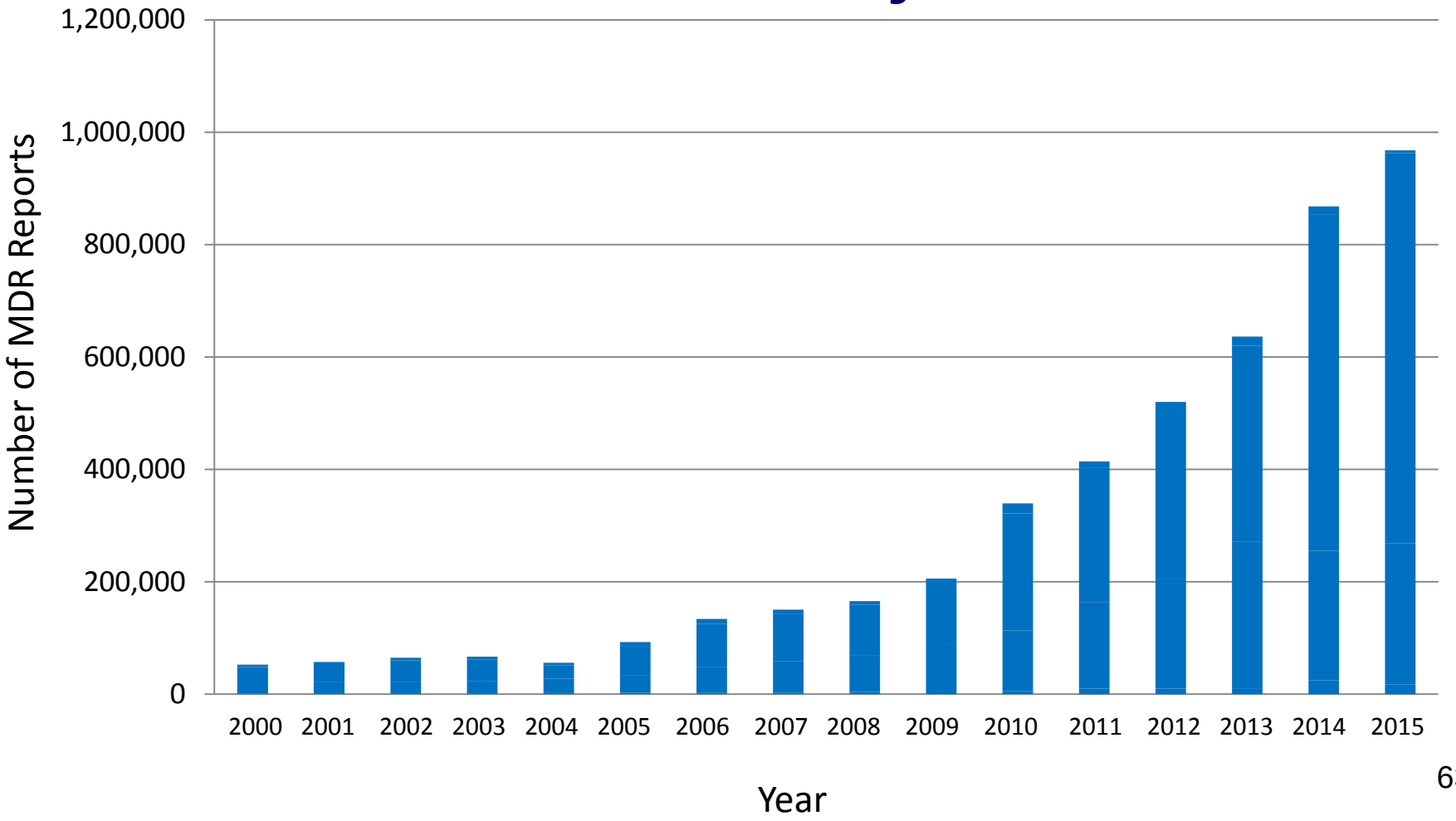
**Center for Devices and Radiological Health**

**June 2, 2016**

# MDR Review Outline and Information Request Letters

- Overview of MDR Reporting
- Limitations of MDRs
- MDR Review of patient infections and/or contamination of heater-cooler devices
- Information Request Letters

# Number of Individual MDR Reports Received by Year



# Events Reported to FDA

## What Types of Events Must Be Reported to FDA?

- If device may have caused or contributed to a death or serious injury
- Certain malfunctions must also be reported by manufacturers/importers

# "Caused or Contributed"

**Death or serious injury was or may have been attributed to a medical device;**

**or**

**A medical device was or may have been a factor in a death or serious injury, including events resulting from:**

- Failure
- Malfunction
- Improper or Inadequate design
- Manufacturing (problems)
- Labeling (problems)
- Use error

# Events Reported to FDA

**A reportable serious injury is defined as:**

**An <u>injury</u> or <u>illness</u> that is:**

- Life-threatening

**<u>or</u>**

- Results in permanent impairment or damage to a body function or structure,

**<u>or</u>**

- Requires medical or surgical intervention to preclude permanent impairment or damage to a body function or structure

# Events Reported to FDA

## When is a Device Malfunction Reportable by the Manufacturer/Importer?

- The device fails to meet its performance specifications or otherwise perform as intended

**and**

- The device is likely to cause or contribute to a death or serious injury if the malfunction were to recur.

# General MDR Reporting

| REPORTER | WHAT TO REPORT | WHERE | WHEN |
|---|---|---|---|
| Manufacturer (Mfr) (Domestic and Foreign) | Deaths, Serious Injuries, Malfunction | FDA | Within 30 calendar days of becoming aware |
| User Facility | Deaths | FDA and Mfr | Within 10 working days of becoming aware |
| | Serious Injury | Mfr (FDA if unknown) | Within 10 working days of becoming aware |
| Importer | Deaths and Serious Injuries | FDA and Mfr | Within 30 calendar days of becoming aware |
| | Malfunctions | Mfr | Within 30 calendar days of becoming aware |
| Voluntary (Patients, Clinicians) | Any type of event | FDA through MedWatch | Any time |

# Limitations of MDRs

- **MDRs are just one of multiple tools used for post market surveillance**
- **MDR analysis results show a snapshot of the reports available at the time the data is pulled, and can change as new information is added and analyzed**
- **Under-reporting**
  - Users unfamiliar with reporting
  - Fear of unintended consequences if they report
  - Confusion about HIPAA privacy and reporting
  - Malfunction or injury may not be clinically apparent

# Limitations of MDRs

- **Limitations of MDR regulation:**
  - Certain device malfunctions may not meet MDR reporting requirements
  - Therefore, **lack of MDRs ≠ lack of problems**

- **Insufficient/Inadequate information in report**
  - Information not obtainable from end user
  - Devices not returned or made available for manufacturer evaluation

- **Inability to Definitively Establish Causality**
  - Cannot determine a definitive link between the use/malfunction of the device and the negative clinical adverse event or outcome.

# MDR Review: Method
## CDRH MDR Database

### MDR Search Criteria

- MDRs related to heater-cooler devices associated with patient infections and/or device contamination
- Date entered into MDR database between January 1, 2010 and February 29, 2016

### Search Results: 180 MDRs

- 146 Manufacturer reports
- 33 User Facility (UF) reports
- 1 Voluntary patient report

# User Facilities and Countries Mentioned in MDR Reports

## Total of 55 User Facilities

**US: 16 UF with 62 MDRs (34%)**

Reports from hospitals in 10 US states

**Outside of the US: 39 UF with 118 MDRs (66%)**

Reports from hospitals in China, Denmark, France, Germany, Netherlands, Switzerland, and United Kingdom

# MDRs by Manufacturer, Brand Name and User Facility (US vs. OUS)

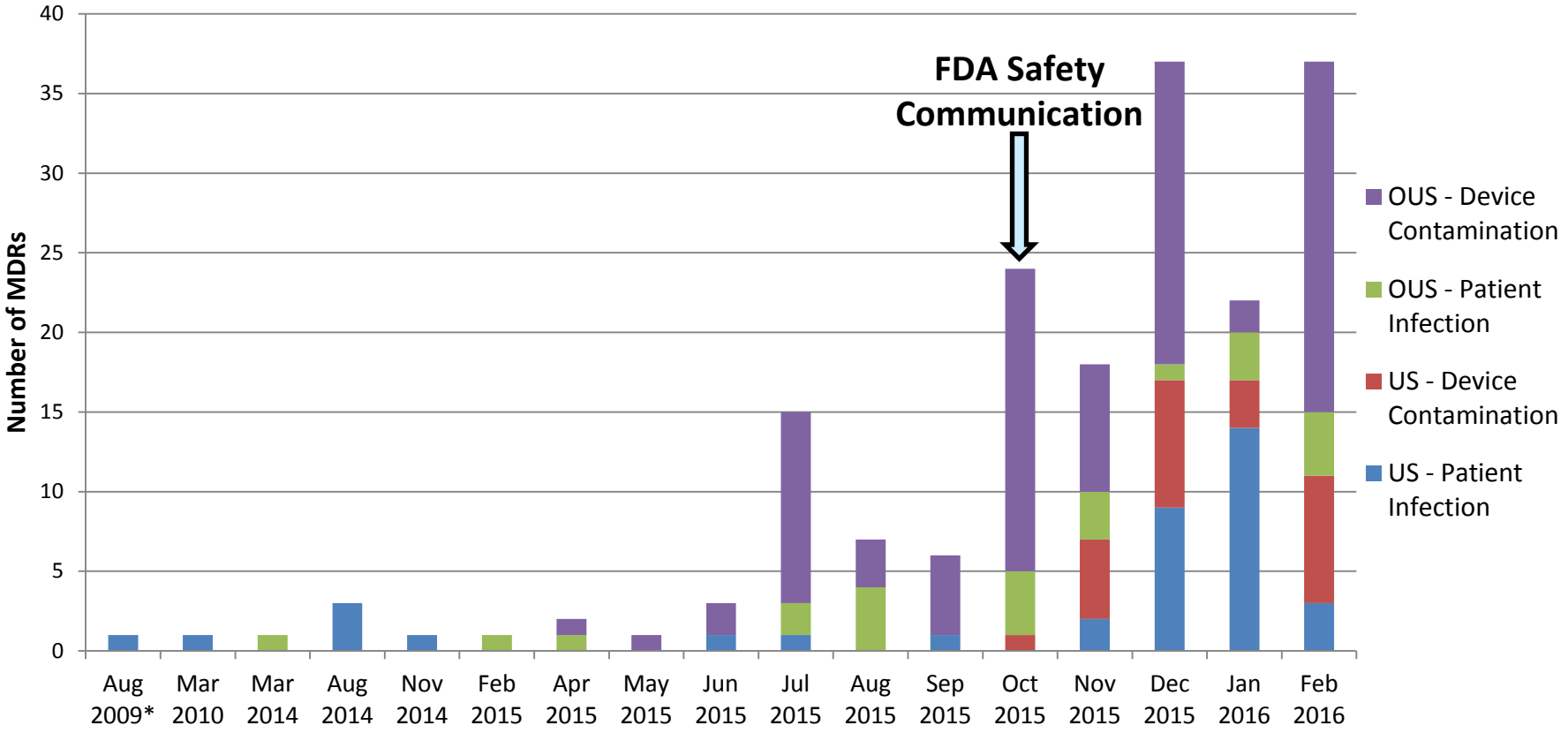
| MDRs by Manufacturer and UF | | | | |
|---|---|---|---|---|
| Manufacturer and Brand Name | Total Number of MDRs | Number of User Facilities Represented in the MDRs | | |
| | | US | OUS | Total |
| LivaNova/Sorin** Stockert 3T | 160 | 15 | 35 | 50 |
| Maquet HCU20, HCU30 & HCU40 | 9 | 0 | 5* | 5* |
| Cincinnati Sub-Zero 333W and Hemotherm | 3 | 2* | 0 | 2* |
| Terumo HX2 | 8 | 1* | 0 | 1* |
| Total | 180 | 16 (2*) | 39 (1*) | 55 (3*) |

*Note that 3 UF reported devices from 2 different manufacturers
**LivaNova/Sorin has approximately 60% of the market share for this type of device

# Heater-Cooler MDRs Associated with Infection/Contamination

## by Date Entered into MDR Database by Month and Year

## N = 180



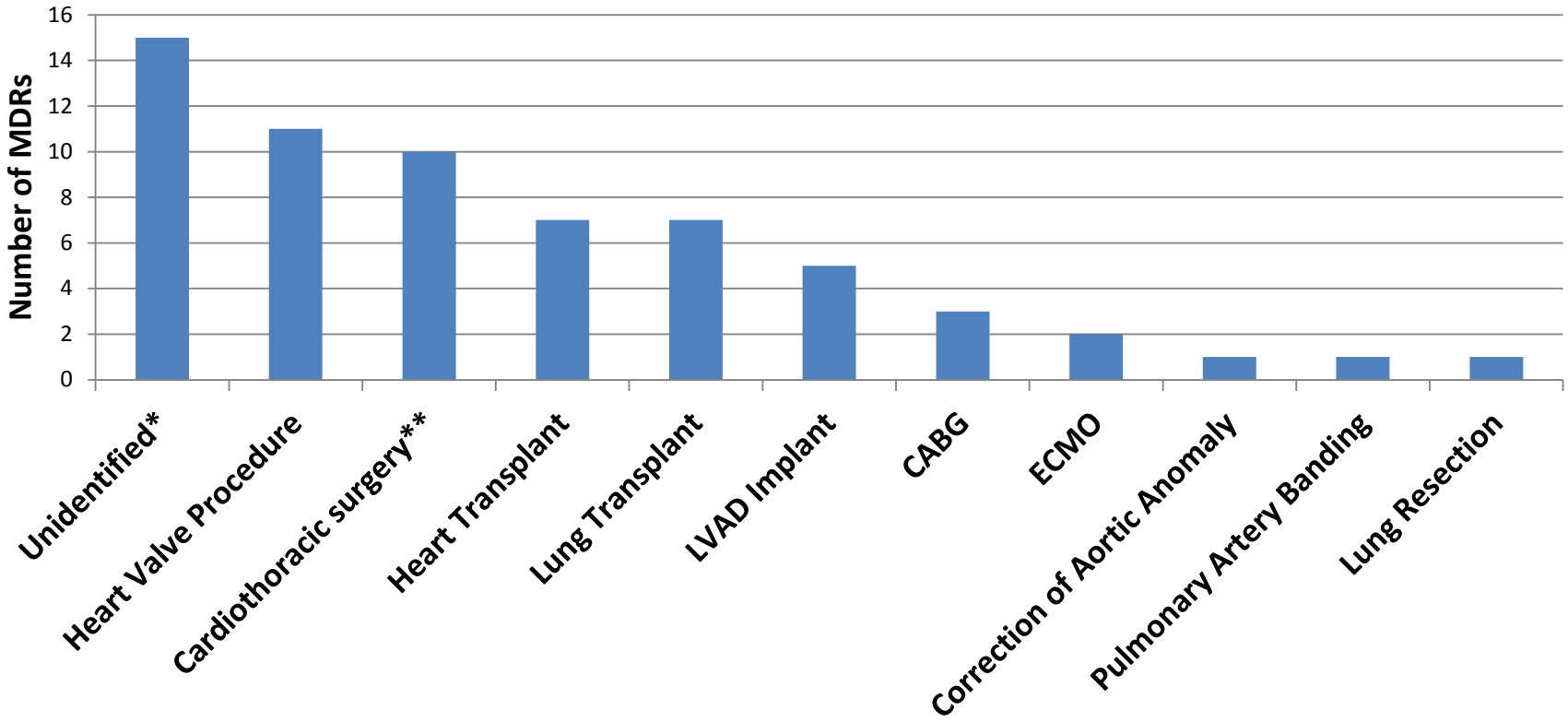

*Note that there was one UF MDR submitted in 2009 related to the March 2010 manufacturer report

# Patient and Device Counts Reported in MDRs by Manufacturer and Brand Name

| Manufacturer and Brand Name | Total Number of MDRs | Infected Patients[1] | | Patient Deaths[2] | | Contaminated Devices[3] | |
|---|---|---|---|---|---|---|---|
| | | US | OUS | US | OUS | US | OUS |
| LivaNova/Sorin Stockert 3T | 160 | 40+ | 21+ | 7+ | 5 | 33+ | 111+ |
| Maquet HCU20, HCU30 & HCU40 | 9 | 0 | 0 | 0 | 0 | 0 | 9 |
| Cincinnati Sub-Zero 333W and Hemotherm | 3 | 1 | 0 | 0 | 0 | 6 | 0 |
| Terumo HX2 | 8 | 4 | 0 | 2 | 0 | 0 | 0 |
| Total | 180 | 45+ | 21+ | 9+ | 5 | 39+ | 120+ |

Note that MDRs may include information on more than one patient and/or device.
[1]Patient infection identifies the total number of patients reported in the MDRs as having an infection.
[2]Patient death identifies the number of patient deaths reported in the MDRs from the number of infected patients.
[3]Device contamination identifies the total number of devices as reported as being contaminated with or without known patient infection.

# Patient Surgical Procedures Identified in the MDRs




**Note that one MDR may include multiple procedures during the surgical intervention.**
*** Surgical procedure was unknown or not identified**
****Unspecified Cardiac/Cardiothoracic Procedure, LVAD (Left Ventricular Assist Device Implant), CABG (Coronary Artery Bypass Grafts), ECMO (Extracorporeal Membrane Oxygenation)**

# Types of Patient Infections as Reported in the MDRs with TTEO

| Diagnosis/Location of Infection | MDR counts | TTEO* Range (months) | TTEO* Mean (months) |
|---|---|---|---|
| Surgical wound infections | 15 | 2.5 - 60 | 46 |
| Unspecified | 13 | 0 - 21 | 11 |
| Endocarditis | 12 | 2.5 - 51 | 26 |
| Blood stream infection | 11 | 0 - 60 | 19 |
| Aortic root abscess | 3 | 10 - 51 | 31 |
| Empyema | 2 | 4 | 4 |
| Abdominal abscess | 2 | 31 | 31 |
| Disseminated infection | 2 | 48 | 48 |
| Driveline infection | 2 | 31 | 31 |
| Muscle flap | 2 | 3 | 3 |
| Mycotic aortic arch pseudoaneurysm | 2 | 10 | 10 |
| Myocutaneous thoracotomy flap infection | 2 | 10 | 10 |
| Pericardial abscess | 2 | 31 | 31 |
| Gastroenteritis | 1 | unk | unk |
| Mitral valve ring infection | 1 | 9 | 9 |
| Septic shock | 1 | 0 - 39 | 20 |

*TTEO is Time to the Event Occurrence when reported in the MDR narrative text.
Note that one MDR may contain multiple infection diagnoses.

# Type of Organism by Manufacturer and Brand Name as Reported in the MDRs

| Type of Organism | LivaNova/Sorin Stockert 3T | Cincinnati Sub-Zero 333W and Hemotherm | Maquet HCU20, HCU30 & HCU40 | Terumo HX2 |
|---|---|---|---|---|
| **All Mycobacteria Total** | 121 | 0 | 5 | 10 |
| *M. abscessus* | 8 | 0 | 0 | 8 |
| *M. avium* | 5 | 0 | 0 | 0 |
| *M. avium intracellulare* | 1 | 0 | 0 | 2 |
| *M. chimaera* | 30 | 0 | 4 | 0 |
| *M. fortuitum* | 1 | 0 | 0 | 0 |
| *M. intracellulare* | 2 | 0 | 0 | 0 |
| Mycobacterium (unspecified) | 53 | 0 | 1 | 0 |
| NTM/Atypical Mycobacteria | 21 | 0 | 0 | 0 |
| **Bacteria (unidentified)** | 26 | 0 | 2 | 0 |
| **Coliform/HPC*** | 2 | 1 | 0 | 0 |
| ***Cupriavidus pauculus*** | 0 | 2 | 0 | 0 |
| ***Legionella sp.*** | 1 | 0 | 0 | 0 |
| ***Pseudomona aeruginosa*** | 1 | 0 | 2 | 0 |
| **Unidentified** | 11 | 0 | 0 | 0 |
| Totals | 162 | 3 | 9 | 10 |

Note that the counts do not equal the number of MDRs as there are cases where multiple organisms may be identified in one MDR.

Welcome and Introduction
Suzanne Schwartz, MD, MBA

Overview of Heater-Cooler Devices
Nicole Milligan, BS

HCD Validation: Cleaning and Disinfection
Elaine Mayhall, PhD

Investigations
Julia Marders, RN, MS

Medical Device Reports
Kelly Bauer, RN, BSN

**Information Request (IR) Letters**
**Kelly Bauer, RN, BSN**

# Information Request Letters

- **Sent to all manufacturers, spec developers, etc.**
- **Focused on the following:**
  - Adverse event reporting to FDA
  - Design aspects that encourage NTM proliferation/biofilm formation, aerosolization
  - Cleaning/disinfection validation
  - Labeling

# Thank you

**This concludes the FDA presentations.**