Disclosure

- Research Associate Professor SUNY Upstate Medical University
- Science Officer Biomedical Simulation Inc.
- Consulting professor XtraCorp Consulting Inc
- I have used medical products off-label in the past
- No financial disclosures

Presentation Outline

- Define off-label product usage
- List examples of off-label ECC product usage
- List the risks and benefits to off-label product use
- Offer a systematic approach to off-label product use
Definition: Off-Label Use of Medical Products

The FDA considers off-label use of medical devices to be “…use [of] a product for an indication not in the approved labeling.”

The FDA also includes the caveat, “…[physicians] have the responsibility to be well-informed about the product, [and] to base its use on firm scientific rationale and sound medical evidence.”

Examples of ECC Off-Label Product Usage

- Extended centrifugal pump use during ECMO
- Warming blanket water supply use during ECMO
- Pushing oxygenators above the rated blood flow during CPB
- Extended oxygenator use during ECMO
- DTI use during ECMO
- DTI use during CPB
- CO₂ diffusers for open heart cardiac surgery
- Homemade metal tip cannulae and connectors
- Femoral cannulae used in internal jugular for venous access
- Failing to clean and disinfect H/Cs per IFUs
- Using MCS cannulae with other centrifugal pumps
- Antithrombin supplement during ECMO / CPB

Off-label use of devices and drugs is common place, reaching estimates as much as 80%.

Perfusion Literature

Learning
- Many aspects to pushing an oxygenator
- Under pressure to reduce homologous blood exposures
- Find an oxygenator AAMI Reference Blood Flow
- Failure model: GME, unable to increase BF if the patient requires

Off-Label Product Usage: Risks vs. Benefits

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<thead>
<tr>
<th>Risks to off-label usage</th>
<th>Benefits to off-label usage</th>
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Systematic approach to off-label use of products

1. Read and understand the manufacturer’s instructions for use, including all warnings
2. Conduct a careful review of the literature regarding the proposed off-label use
3. Consult with other clinicians who have used the product off-label
4. Design your own test of change using PDSA or DMAIC
5. Complete a failure mode and effect analysis (FMEA) for the expanded off-label use
6. Consult your institutional review board for local guidelines

Off-Label Product Usage: Risks vs. Benefits

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<td>Physician prescribers are not always aware – be sure they understand</td>
<td>Provide life-saving or adaptive care to patients with unique or emergent needs</td>
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<td>Patient harm is possible especially in the absence of evidence of efficacy</td>
<td>Apply for compassionate use of devices qualified with FDA for other indications</td>
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<tr>
<td>Failure to respect the manufacturer’s investment to qualify a product for safety with the FDA</td>
<td>Able to continue team and patient education, and promote scientific discovery</td>
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<td>Failure to consider the moral and ethical challenges, and the potential quagmire</td>
<td>Decrease cost of care</td>
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Definition: Off-Label Use of Medical Products

Suggested reading

Summary – Quote Mr. Myers

“Understanding and using manufacturer IFUs to guide us in our clinical practice should never replace a professional’s clinical judgment, but at the same time, they [IFUs] should not be taken for granted and challenged in a clinical scenario without fully understanding the IFUs and any potential negative implications to our patient population.”

Gerard J. Myers. JECT. 2014;46:192-196
What’s New with Heater-Coolers: 2018 to Present

Al Stammers

What have we learned over the last 15 months concerning heater-cooler borne infections?

What new guidelines exist?


Objectives

- Slow-growing nontuberculous mycobacterium (NTM)
- Belongs to M. avian complex (MAC)
- First reported in 2004 in medical situations
- Ubiquitous - found in water, dust and soil samples
- Concentrates in biofilms
- Opportunistic with immunocompromised and open surgical procedures especially vulnerable

Mycobacterium chimaera
At least a dozen children who had heart surgery at Children’s Hospital New Orleans between late May and July have infected incisions, apparently from contaminated equipment.

The infections were linked to a machine that regulates a patient’s temperature during heart surgery.

“...at least three other companies’ devices have also been linked to bacterial contamination worldwide, and both the FDA and CDC have acknowledged that the concern goes beyond any one brand.”
Scientific Publications
- Case reports, clusters (4)
- Genomics (1)
- Disinfection, monitoring (5)
- ECMO (1)
- Non-LivaNova HCD Infections (2)
- Country Reports (5)
- Miscellaneous (8)

Follow all manufacturer’s current instructions for cleaning and disinfection
- Establish training/competencies for individuals tasked with maintenance
- Establish and maintain a log for each HCD for cleaning and disinfection
  - Date and time of cleaning
  - Individual(s) who performed the cleaning
- Maintenance has 100% requirement
- Report suspected HCD infections to the FDA via MedWatch

Competency Assessment
✓ Assures consistency across personnel
✓ Documents conformity
✓ Regular reviews and updates on new information/directions

Analytics to Track Disinfection

PubMed Search March 5, 2019
26 Reports
Recent Developments

On October 19, 2018, the FDA issued a safety communication to provide updated information to mitigate potential cardiac surgery infection risks associated with the LivaNova 3T Heater-Cooler Systems.

On June 12, 2018, the FDA issued an updated safety communication to amplify LivaNova’s Medical Correction issued on April 20, 2018.

On October 19, 2018, the FDA issued a safety communication to provide updated information to mitigate potential cardiac surgery infection risks associated with the LivaNova 3T Heater-Cooler Systems.

June 12, 2018

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

LivaNova’s Deep-Cleaning Service for 3T HCD < 10 years old
- 3T HCD with known or suspected NTM contamination
- 3T HCD manufactured before September 2014
- 3T HCD manufactured after September 2014 w/o NTM

Pre-September 2014 3T HCD
- "Strongly consider transitioning away from the use of these devices for open-chest cardiac surgery unless your device has successfully been deep cleaned by LivaNova."
• Follow the Daily Hydrogen Peroxide Monitoring Instructions.

Users should monitor the hydrogen peroxide concentration in the water solution on a daily basis to verify that sufficient concentration of hydrogen peroxide is present in the water circuit of the device. A decrease in hydrogen peroxide over the 7-day period until the next water change is expected, however the hydrogen peroxide concentration should remain above 100 ppm.

• Be aware of the 3T Design Upgrade.

LivaNova has developed a vacuum canister and internal sealing design change that is intended to further reduce, but does not eliminate, the risk of airborne transmission of non-tuberculosis mycobacterium (NTM) from the 3T device.
Vacuum & Sealing Upgrade

- Hygiene Controls
- Disinfection Protocols & Validation
- Drying process & validation

Surgical Field Placement

- Initial Disinfection in Operating Instructions
- Vacuum & Sealing Upgrade
- Surgical Field Placement

Routine cleaning/disinfection in OI
- Deep disinfection process

Heater-Cooler Update

- Over 26 new reports over last 15 months on heater-cooler borne infections
- Reports of infections will continue and heater-cooler devices have now ‘made the grade’
- Deep cleaning and disinfection processes cleared by FDA for LivaNova 3T devices, and retrofit processes available for existing units

Thank You

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