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Cleaning and Sterilization of Used Cardiac Implantable Electronic Devices With Process Validation

The Next Hurdle in Device Recycling

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ABSTRACT

OBJECTIVES This study sought to develop a validated, reproducible sterilization protocol, which could be used in the reprocessing of cardiac implantable electronic devices (CIEDs).

BACKGROUND Access to cardiac CIED therapy in high-income and in low- and middle-income countries varies greatly. CIED reuse may reduce this disparity.

METHODS A cleaning and sterilization protocol was developed that includes washing CIEDs in an enzymatic detergent, screw cap and set screw replacement, brushing, inspection, and sterilization in ethylene oxide. Validation testing was performed to assure compliance with accepted standards.

RESULTS With cleaning, the total mean bioburden for each of 3 batches of 10 randomly chosen devices was reduced from 754 to 10.1 colony-forming units. After sterilization with ethylene oxide, with 3 half-cycle and 3 full-cycle processes, none of the 90 biological indicator testers exhibited growth after 7 days. Through cleaning and sterilization, protein and hemoglobin concentrations were reduced from 99.2 to 1.42 $\mu g/cm^2$ and from 21.4 to 1.03 $\mu g/cm^2$, respectively. Mean total organic carbon residual was 1.44 parts per million (range 0.36 to 2.9 parts per million). Endotoxin concentration was not detectable at the threshold of <0.03 endotoxin units/ml or <3.0 endotoxin units/device. Cytotoxicity and intracutaneous reactivity tests met the standards set by the Association for Advancement of Medical Instrumentation and the International Organization for Standardization.

CONCLUSIONS CIEDs can be cleaned and sterilized according to a standardized protocol achieving a 12-log reduction of inoculated product, resulting in sterility assurance level of 10^{-6}. (J Am Coll Cardiol EP 2017;■:■-■)

Cardiac implantable electronic devices (CIEDs)—pacemakers and implantable cardioverter-defibrillators (ICDs)—have had a major impact on improvements in the quality of life and longevity of patients with cardiovascular disease (1-3). Implantation rates of CIEDs have increased in recent decades in the United States and other high-income countries (4). Unfortunately, CIEDs are

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ABBREVIATIONS AND ACRONYMS

AAMI = Association for the Advancement of Medical Instrumentation

ANSI = American National Standards Institute

BI = biological indicator

CIED = cardiac implantable electronic device

CJD = Creutzfeldt-Jakob disease

CRT-D = cardiac resynchronization therapy-defibrillator

FDA = Food and Drug Administration

ICD = implantable cardioverter-defibrillator

ISO = International Organization for Standardization

LMIC = low- and middle-income country

PCD = process challenge device

RO/DI = reverse osmosis/deionized

unavailable for many patients in low- and middle-income countries (LMICs), mainly because of the expense associated with this therapy, but also because of the underdevelopment of the health care infrastructure (5). It has been suggested that post-mortem collection and evaluation of CIEDs may be a means of improving access to brady- and tachy-therapies for patients, who are otherwise denied these lifesaving therapies (6,7). However, device reuse remains controversial, and serious concerns about the safety of this practice remain (3,8–10). Increased risk of infection with a reused pacemaker or ICD is a major concern with CIED reuse.

Although pacemaker and ICD reconditioning has been described as a safe method for delivering electrophysiological health care, a blueprint for safe CIED reprocessing is lacking (7,11,12). We have developed a protocol to clean and sterilize CIEDs, and present the protocol along with validation of the process. This represents one key step in our efforts to safely and effectively recycle used CIEDs.

METHODS

REPROCESSING. Receipt and inventory. As previously described, CIEDs were collected at funeral homes and crematories according to instructions available at http://www.med.umich.edu/myheartyourheart/index.htm (13). CIEDs with a dented housing or any broken parts were rejected and discarded. CIEDs that passed visual inspection were wiped with Lysol, sorted by manufacturer, interrogated for battery longevity, and logged into a CIED register. An overview of the product workflow is shown in **Figure 1**. An abbreviated reprocessing protocol is presented here. Detailed description can be found in Online Appendix Section 1.

In order to develop methods to clean and sterilize devices, we selected an assortment of contemporary CIEDs, ranging from small pacemakers to large cardiac resynchronization therapy-defibrillators (CRT-Ds), representative of 3 manufacturers (Boston Scientific, Medtronic, and St. Jude Medical). Online Table 2.1 lists the device types and models presented for reprocessing.

Cleaning and decontamination. CIEDs were placed side by side in a reverse osmosis/deionized (RO/DI) water sink and soaked for 10 minutes in Enzol enzymatic detergent solution (Advanced Sterilization Products, Irvine, California).

Brief battery retest. CIED outputs were connected to a 500-ohm test load. The devices were set to a predetermined test configuration: 1) mode: DDD (or VVI for single-chamber devices); 2) pacing output: 2.5 V at 1.0-ms pulse width; 3) pacing rate: 60 pulses per min; 4) any other sensors or device features turned off. Battery condition was noted to determine if there was sufficient longevity based on pre-determined qualification criteria (4 years or >75% of the original battery life remaining). CIEDs were then configured to storage settings: 1) mode OFF; 2) if mode OFF was not available: DDD/VVI for dual-/single-chamber devices with pacing output (atrium and/or ventricle) set to 1.0 V at 0.1 ms, pacing rate 30; 3) all other parameters and sensors turned OFF.

Screw cap (seal plug) and set screw removal. Using a sharp blade and a lighted magnifying glass, all screw covers were removed from the header. Set screws were removed from connector ports and inspected. Retained screw caps and set screws were rinsed in distilled water, wiped dry, sorted, and stored by manufacturer.

Initial cleaning. Forty CIEDs were placed side by side in an RO/DI sink and soaked for 3 minutes in Enzol solution. Set screws and seal plug were soaked in the enzymatic cleaner in a small container.

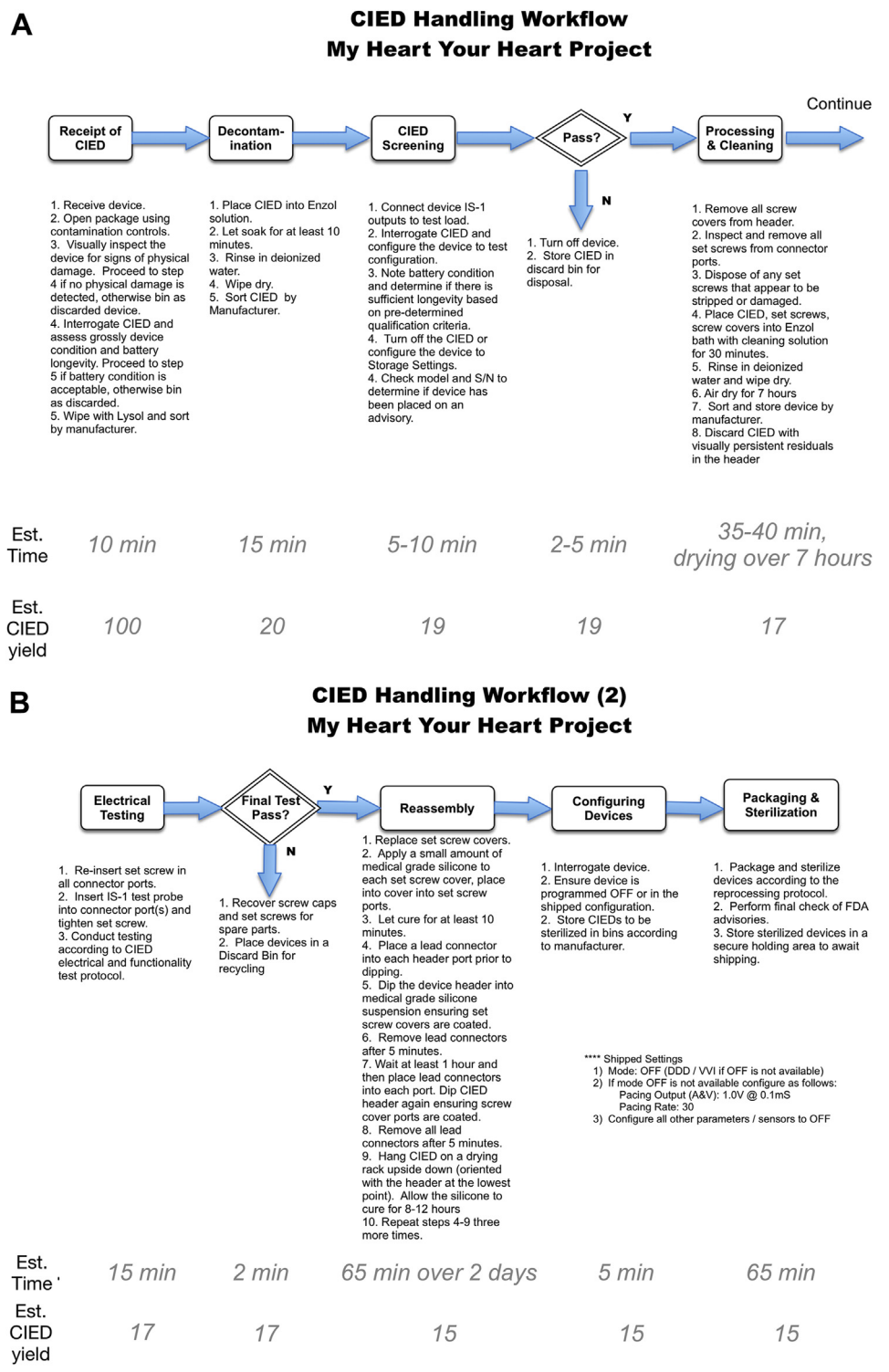
Wiping and brushing of devices. The CIEDs were wiped 4 times, including the header, with a lint-free towel. Any crevices on the housing and near the header were cleaned with a nylon brush. Pipe cleaner brushes were inserted into the connector ports in the header of the device, rotated 360°, and removed. Each part of this step was repeated 4 times. The entire CIED was then gently cleaned with 6 strokes of a nylon brush while under the water's surface. Lead connector ports were inspected using a 5× magnifier glass. If any debris was found, the entire wiping process was repeated. If debris still remained after 2 wiping and brushing cycles, the CIED was discarded. The batch of 40 CIEDs was then pressure rinsed for 20 to 40 s with warm tap water.

Emersion soak rinsing. Forty CIEDs were placed in the process basket and into an RO/DI sink with approximately 3 gallons of (RO/DI) water. After 3 minutes, the sink was drained. Immersion soak rinse was repeated 3 times. After the third rinse cycle, CIEDs were visually inspected for any damage. Any damaged devices were discarded. Set screws and seal plugs were handled in the same fashion.

Drying. CIEDs, set screws, and seal plugs were placed in the vacuum drying chamber and dried in a vacuum at 35°C to 50°C for 7 h.

Set screw reassembly and electrical test. All set screws and silicone set screw covers were visually

FIGURE 1 **Production Workflow for Reprocessing CIEDs by Project My Heart Your Heart**



(A) Initial stages or reprocessing from receipt of CIED to its cleaning. **(B)** Device handling starting with electrical testing to final cleaning, packaging, and sterilization. Estimated time needed to complete each step of the protocol per device and estimated yields at each step are also shown. The skill of the operator and processing in batches of 40 devices result in significant time savings. CIED = cardiac implantable electronic device; FDA = Food and Drug Administration.

inspected to ensure that there was no visible blood remaining on the parts. A reference connector pin was inserted into the header port. The appropriate set screw (according to the manufacturer) was inserted into each connector block. Using a no. 2 torque wrench, each set screw was inserted into the connector port. The set screw was then backed off 1.5 turns to ensure that it was positioned correctly to allow a lead connector to be inserted into the header, yet not too far out to risk disengagement with the connector block. If the set screw bound up or could not be advanced within the connector block, the screw was replaced, and the damaged set screw was discarded. Electrical testing was conducted per electrical test protocol.

Screw cap reassembly. A hex wrench was inserted into a reconditioned set screw cover. A small amount of silicone fluid was applied on opposite sides of the seal plug. The appropriate set screw cover (according to the manufacturer) was inserted into each set screw port. All pacemaker headers were dip coated to seal and secure the screw covers in place in the header. The header was dipped into the silicone fluid just enough to cover all screw covers. The CIEDs were hung (with the header positioned down) on a drying rack, and the dipping process was repeated after 1 h. The silicone was allowed to fully cure for 12 to 24 h. The dipping process was repeated 3 times. The reassembled CIEDs then were placed into a clean closable bin, labeled with the lot number, and transferred for inspection and packaging.

Inspection and packaging. During inspection, CIEDs were rejected for any of the following reasons: cracks, damage, deformity, or any abnormality suggesting that function of the device might be compromised. Pouch labels were printed and applied, and each device was put into a pouch, heat sealed, and staged for sterilization. Reprocessed pacemakers were packaged in a 5.25-inch × 15.00-inch Tyvek peel pouch (1073B and nylon/low-density polyethylene/ethylene vinyl acetate; DuPont, Wilmington, Delaware).

Sterilization. The CIEDs were sterilized and aerated in accordance with American National Standards Institute/Association for the Advancement of Medical Instrumentation/International Organization for Standardization (ANSI/AAMI/ISO) 11135-2007 using 100% ethylene oxide in a Steri-Vac 8XL Sterilizer chamber (3M, St. Paul, Minnesota) (14). After chamber ethylene oxide exposure, the biological indicators (BIs) were removed from the load and incubated, and the load was moved to an aeration chamber for 48 h. The sterilization load was quarantined while the BIs completed incubation.

VALIDATION TESTING: STERILIZATION. Native soil: bioburden testing. In order to assure that the cleaning and sterilization process is effective in reducing the bioburden on devices, we conducted microbial limit testing on 2 populations of CIEDs before sterilization: 1) uncleaned CIEDs that had undergone artificial soiling; and 2) cleaned CIEDs. Artificial soiling is the application of an organic load and bioburden onto medical devices. The purpose of artificial soiling is to demonstrate that the cleaning and sterilization procedure is capable of effectively removing large amounts of organic material, which may not be present on randomly selected test devices. For each of the 2 CIED populations, 3 lots of 10 CIEDs were evaluated for bioburden before sterilization. The uncleaned CIEDs were inoculated with an organic soil of 50g/l bovine serum, 50 ml/l sheep blood, and 10 g per liter pork mucin. These quantities are reflective of the worst case levels found to remain on medical devices or instruments after patient use but before reprocessing. The CIEDs were accelerated aged for 2.2 days at 60°C (15). Subsequently, the 3 lots of uncleaned, soiled, unsterilized CIEDs ($n = 30$) and the 3 lots of cleaned, unsterilized CIEDs ($n = 30$) were tested for aerobic bacteria, yeast, and mold bioburden using the membrane filtration method (16).

BI sterility testing. BIs were chosen according to AAMI/ISO 14161 (17). Commercially made self-contained BIs from 3M (Attest) and STERIS (Verify and Spordex) containing spores of *Bacillus atrophaeus* (*Bacillus subtilis* var. niger) were used for sterilization validation. The BIs were placed with the CIEDs, and process challenge devices (PCDs) were placed in an ethylene oxide sterilization chamber along with the pouched CIED/PCD combination. Methodology was followed according to ANSI/AAMI/ISO 11737-1 (16). All 20 PCD BIs along with a control BI were incubated to verify proper growth conditions. CIEDS and PCDs were then subjected to half-cycle sterilization.

Three separate half-cycle tests and 3 separate full-cycle tests were performed (14). Each BI was contained within the PCD. All validation runs were incubated for 7 days.

VALIDATION TESTING: RESIDUAL ORGANIC SOIL. Protein and hemoglobin. A total of 10 reprocessed devices (3 small Guidant Insignia pacemakers and 7 large Guidant CONTAK RENEWAL-3 CRT-Ds [Guidant, Redmond, Washington]) were selected at random. Each of the small pacemakers was placed in a small plastic Stomacher bag containing 40.8 ml of the extraction fluid. Each of the larger CRT-Ds was placed in a Stomacher bag containing 105.8 ml of the extraction fluid. The bags with CIEDs were sonicated

for 15 minutes and then gently shaken for 1 min before sampling. Organic soils were then assayed using commercially available laboratory methods: Pierce bicinchoninic acid (BCA) total protein assay (Thermo Scientific, Rockford, Illinois) and Bioassay Systems QuantiChrom total hemoglobin assay (Bioassay Systems, Hayward, California). Details of the protocol of protein and hemoglobin analysis can be found in Online Appendix Section 2.

Total organic carbon residual. Ten CIEDs were extracted in 40 ml of sterile water for injection contained in Ultraclean EPA TOC vials (VWR International, Radnor, Pennsylvania). The samples were sonicated for 10 min in the ultrasonic cleaner, then vortexed for 60 seconds before sampling. The extracts were analyzed by Boston Analytical, Inc. (Salem, New Hampshire) according to USP 32 <643> (18).

VALIDATION TESTING: BIOCOMPATIBILITY. Biocompatibility testing was performed by Mycoscience Laboratories (Willington, Connecticut) and Moog Medical Device Group (Rush, New York) in accordance with appropriate standards for biological evaluation of medical devices using International Organization for Standardization (ISO) methods for elution (extract), intracutaneous reactivity, protein and hemoglobin residuals, total organic carbon, and pyrogenicity (17–19).

Cytotoxicity/minimal essential medium elution. Ten reprocessed devices underwent cytotoxicity testing using the minimal essential medium elution method (17,18). Extractions were conducted at 37°C for 24 h using mammalian cell culture media (minimal essential medium with 5% serum). The extracts were plated on monolayer mouse fibroblast cells (L929) and incubated. High-density polyethylene extract functioned as negative control, and sterile latex rubber extract was the positive control. Sample and control plates were run in triplicate. After incubation, the cells are examined microscopically for malformation, degeneration, and lysis of the cells. Quantitative morphological grading of cytotoxicity from grade 0 (discrete intracytoplasmatic granules, no cell lysis, no reduction in growth) to grade 4 (nearly complete or complete destruction of the cell layers) (20,21). Details are given in Online Appendix Section 2.

Intracutaneous reactivity. Ten reprocessed CIEDs were analyzed based on previously published standards (17,19). Extraction was performed with polar solvent (saline) and nonpolar solvent (cottonseed vegetable oil) by submerging the entire device for 73 h at 37°C ± 1°C. Three healthy young adult albino rabbits were injected intracutaneously at 5 sites with 0.2 ml of test extract and at 5 sites with the corresponding blank. The sites were examined immediately after injection, at 24 ± 2 h, 48 ± 2 h, and 72 ± 2 h after injection for gross evidence of tissue reaction, such as erythema or edema. Each area was scored from 0 to 4.

Pyrogenicity. The test was conducted under worst case conditions using the Limulus amebocyte lysate method. Each of the 10 samples was extracted with 100 ml per device of pre-warmed 37°C sterile water for injection. Limulus amebocyte lysate reagent and *Escherichia coli* 0113 endotoxin were used (Associates of Cape Cod, East Falmouth, Massachusetts). The resultant eluate was then tested per the U.S. Food and Drug Administration (FDA) method using a lysate sensitivity of 0.03 endotoxin unit/ml (22).

Ethylene oxide and ethylene chlorohydrin residues. After 2 full reprocessing and sterilization cycles, 10 CIEDs were tested for ethylene oxide and ethylene chlorohydrin residues. After exposure, devices were aerated for 3 h and frozen until testing. The sampled CIEDs were tested in accordance with ANSI/AAMI/ISO 10993-7 Biological Evaluation of Medical Devices-Part 7: Ethylene Oxide Sterilization Residuals (23). CIEDs were extracted by immersing them in 100 ml deionized water for 24 h at 37°C. The extraction fluid then was analyzed with an HP 6890 gas chromatograph (Hewlett-Packard, Palo Alto, California).

RESULTS

The results for bioburden, BI sterility testing, protein and hemoglobin residuals, total organic carbon, cytotoxicity, intracutaneous reactivity, pyrogenicity, and ethylene oxide and ethylene chlorohydrin residues are given in **Table 1**. Included in the table are acceptable thresholds for each test (if defined), reference documents providing regulatory guidance for reprocessing of medical devices, and references to the specific parts of the Online Appendix, which contains detailed results of the validation.

DISCUSSION

The main finding of this study was that CIEDs may be cleaned and sterilized under a comprehensive protocol resulting in sterility assurance level of 10^{-6}, a common standard for reusable medical devices. The protocol is effective in removing protein and hemoglobin residuals, as well as organic carbon, meeting the AAMI TIR-30 guideline acceptance criteria (15). Reprocessed CIEDs satisfied biocompatibility standards according to ISO 10993 Biological Evaluation of Medical Devices in terms of cytotoxicity, intracutaneous reactivity, pyrogenicity, and ethylene oxide residuals (19).

TABLE 1 Results of CIED Cleaning and Sterilization Validation Including Acceptable Criteria, Reference Documents, and References to the Online Appendix with Detailed Information for Each Test

Tests Performed	Results	Acceptable Criteria	Reference Documents	Full Results
Native soil: bioburden testing	Total mean bioburden for uncleaned, artificially soiled CIEDs: 762 CFUs, 297 CFUs, and 1,204 CFU Total mean bioburden for cleaned, unsterilized devices: 6.2 CFUs, 5.6 CFUs, and 18.6 CFUs	There is no absolute cutoff value for this test. Tested mean bioburden is compared to the BIs used in routine sterilization, which have approximately 38.6 million spores. If sterilization reliably inactivates BI with 38.6 million spores, it is capable of killing a few hundred or even thousand CFUs.	ANSI/AAMI/ISO 14161 (17)	Online Tables 3.1 and 3.2
BI no growth testing	No growth in 120 samples at max 168 h	No growth in all samples at 168 h	ANSI/AAMI/ISO 14161 (17) ANSI/AAMI/ISO 11737-1 (16) ANSI/AAMI/ISO 11135-1 (14)	Online Tables 4.1, 4.2, 4.3, 4.4, 4.5, and 4.6
Protein residual	Mean 1.42 μg/cm^2 (range 1.08–2.1 μg/cm^2)	≤6.4 μg/cm^2	AAMI TIR-30 (15)	Online Table 5.1
Hemoglobin residual	Mean 1.03 μg/cm^2 (range <0.9–1.4 μg/cm^2)	≤2.2 μg/cm^2	AAMI TIR-30 (15)	Online Table 5.1
Total organic carbon	1.45 ppm (range 0.36–2.9 ppm)	<12 ppm	USP 32 <643> (18)	Online Table 5.2
Cytotoxicity (0 = no cell lysis, 4 = complete destruction of cell layers)	0 (nonreactive) at 24 and 48 h	0 (nonreactive) at 24 and 48 h	ISO 10993-5 (29)	Online Table 5.3
Intracutaneous reactivity (0 = no reactivity, 4 = edema/erythema)	Overall mean test score 0–0.6	There is no absolute cutoff score for passage of this test.	AAMI TIR-30 (15) AAMI TIR-12 (30)	Online Table 5.4
Pyrogenicity: Limulus amebocyte lysate method	<0.03 EU/ml or <3.0 EU/device	<0.5 EU/ml or 20 EU/device	ANSI/AAMI/ISO 10993-11 (31) FDA guidance for industry: pyrogen and endotoxins testing: questions and answers (22)	Online Table 5.5
Ethylene oxide and ethylene chlorohydrin residues	<0.100 mg/device for ethylene oxide and <0.100 mg/device for ethylene chlorohydrin	<4 mg/device for ethylene oxide and <9 mg/device for ethylene chlorohydrin	ANSI/AAMI/ISO 10993-7 (23)	Online Table 5.6

AAMI = Association for the Advancement of Medical Instrumentation; ANSI = American National Standards Institute; BI = biological indicator; CFU = colony-forming unit; CIED = cardiac implantable electronic device; EU = endoxotoxin unit; FDA = Food and Drug Administration; ISO = International Organization for Standardization; ppm = parts per million; USP = United States Pharmacopeia.

Pacemakers and ICDs are approved by the U.S. FDA and the European Union's National Competent Authorities as single-use devices. Although patients in the United States and European Union are almost always able to receive a pacemaker or ICD they need, many patients in LMICs do not have the same access to these therapies because of the prohibitive cost of new devices. CIEDs harvested from the deceased or from patients undergoing device upgrades in high-income countries could improve access to these lifesaving therapies for patients in LMICs (13,24). To our knowledge, there have been no published comprehensive protocols for reprocessing CIEDs. In this paper, we propose a detailed step-by-step method to clean and sterilize previously implanted CIEDs. We also present validation of our sterilization protocol. Electrical and functionality testing, additional key components of CIED quality assurance, will be addressed in subsequent reports.

Pacemaker and ICD pulse generators are enveloped by a biocompatible titanium alloy casing and a polycarbonate transparent connector (header). The leads are inserted into hollow header ports, which contain set screws. Seal plugs (septa) are intended to protect the set screws and minimize fluid intrusion. During and after implantation, however, blood and body fluids may seep into the header ports through the seal plugs. Removal of this potential contaminant requires removal of the seal plugs and set screws. Our protocol demonstrates the feasibility of seal plug and set screw removal and their replacement.

There are unique challenges associated with cleaning and sterilizing a device that is not intended for reprocessing. Chronically implanted devices are covered by biofilm that, like "rocks in a stream," can prevent complete removal of the biological contaminant. Bacterial cells produce extracellular polymeric substances and are held together by these strands, allowing them to develop complex 3-dimensional, resilient, attached communities. In order to mitigate any uncertainty regarding our ability to remove biofilm from devices, we performed additional soiling of CIEDs and validated the cleaning and sterilization protocol using worst case scenarios.

A common concern among physicians regarding CIED reuse is potential transmission of hepatitis C or

human immunodeficiency virus. Both viruses consist of a lipoprotein envelope surrounding the nucleic acids, making them particularly susceptible to enzymatic cleaners. Previous studies involving a general-purpose detergent, an enzymatic cleaner, and sterilization with ethylene oxide showed inactivation of the infectious particles on cardiac electrophysiology catheters (25,26). These and other studies suggest the risk of infection with hepatitis C or human immunodeficiency virus with CIED reuse is exceedingly unlikely.

The findings presented in this paper are part of the various aspects of CIED reuse our group has been systematically working on. Our goal is to create a blueprint for safe CIED reuse as a means of addressing the gaping disparity in access to pacemakers and ICDs between high-income countries and LMICs. We demonstrated that large-scale CIED collection from funeral homes and crematories is feasible (13). In our experience, approximately 20% of all CIEDs collected from the funeral home industry have at least 75% of the original battery, or at least 4 years of remaining estimated longevity, although the yield for CRT devices is as high as 30% (13). We created a website (http://www.myheartyourheart.org) to allow funeral homes, crematories, and individuals to request postage-paid envelopes and biohazard bags, which are in compliance with U.S. Department of Transportation shipping laws. Through a network of partnerships with funeral home and crematory directors, the Michigan Funeral Home Director Association, and Implant Recycling, LLC. (Detroit, Michigan), we have been able to collect approximately 3,000 devices that meet our threshold for battery requirement.

The University of Michigan is at the center of interactions with various entities beyond the funeral industry: nonprofit organizations, Pan African Society of Cardiology, American Pakistani Cardiology National Association, and pacemaker implantation centers in LMICs. We have partnered with World Medical Relief, Inc., a Detroit-based nonprofit organization, which donates medical equipment and supplies to LMICs. As the project grew, World Medical Relief has provided us the necessary space to continue the procurement, evaluation, and storage of CIEDs at various stages of reprocessing. Although other successful donation programs of previously used pacemakers and ICDs have been reported (11,12), our effort is different because we chose to reprocess the devices within the United States, where we exercise complete control over the entire process of device evaluation and refurbishing. Because of the specialized nature of the cleaning and sterilization process, we have partnered with NEScientific (Waterbury, Connecticut), a company with expertise in reprocessing medical devices and instruments. Because our CIEDs are reprocessed within the United States, the FDA regulates their transfer abroad as it regulates interstate commerce (27). The CIEDs we reprocess no longer adhere to the original equipment manufacturer's specifications. Data focusing on cleaning and sterilization, which are presented in this paper, were part of the application to the FDA. All countries for which the FDA has issued us an export permit had expressly approved the importation of the CIEDs. In several counties spanning 3 continents, we are poised to start enrollment in a pivotal study of safety and efficacy of reused pacemakers. World Medical Relief will provide the logistical support for our overseas operations. LMIC implantation centers will screen potential patients ensure they meet the clinical need and can demonstrate indigenous status. My Heart Your Heart will provide pacemakers without charge. New leads necessary for implantation of the refurbished pacemakers will be donated. We have filed for My Heart Your Heart to become a 501(c) (3) nonprofit organization to allow fundraising. Our rough estimate is that the cost of reprocessing a pacemaker is approximately $60 to $80, contingent on our ability to scale up the project to several hundred devices per year in the midterm. To date far the entire work has been accomplished with volunteer assistance.

Patients will receive the donated devices only after providing full informed consent. If safety and efficacy can be established to the satisfaction of the professional societies and regulatory bodies, further partnerships and models for collaboration can be developed, and the initiative can be scaled up for maximum benefit of the underserved population. The reproducibility of our effort will depend in part on how successful we are in the reprocessing of CIEDs, implementation of the clinical study, and the ability to gain financial support. If reuse is to become a viable approach to address the lack of access to CIEDs in LMICs, an accepted quality standard for all the steps in device reprocessing is needed.

STUDY LIMITATIONS. Although this study provides some basic confirmation that many CIEDs can be cleaned and sterilized, these results may not be reproducible in all kinds of pacemakers and ICDs. Removal of the seal plugs and set screws allows for proper cleaning of the device header but raises the possibility of functional failure. An electrical test is

essential to assure proper function of the set screw after the cleaning proposed in this study but is beyond the scope of this study.

Whether our reprocessing could inactivate the causative agents of spongiform encephalopathies such as scrapie, bovine spongiform encephalopathy, and Creutzfeldt-Jakob disease (CJD) is unknown. However, all known cases of iatrogenic CJD to date have resulted from exposure to the elements of the central nervous system or the eye tissue. No known cases of CJD are attributable to the reuse of devices contaminated with blood or to the transfusion of blood products (28).

CONCLUSIONS

CIEDs may be cleaned and sterilized according to a standardized protocol, resulting in sterility, significant reduction in residual in residual organic soil, and satisfaction of the biocompatibility standards for medical reusable devices. Before CIEDs may be offered for reuse, electrical and functionality tests must be performed in order to assure a minimum level of safety.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: There is a great disparity in access to CIED therapy between high-income and LMICs. CIED reuse may reduce this disparity. A protocol, which includes washing of CIEDs in an enzymatic detergent, screw cap and set screw replacement, and sterilization in ethylene oxide, is shown to result in compliance with accepted standards of sterility for medical device reprocessing.

TRANSLATIONAL OUTLOOK: Further research is needed to develop comprehensive electrical testing protocols to assure that CIED reuse is safe. Additionally, clinical outcomes data from prospective studies may show safety and efficacy of CIED reuse.

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KEY WORDS **implantable cardioverter-defibrillator, pacemaker, recycling, reuse, sterilization**

APPENDIX **For an expanded Methods section as well as supplemental tables, please see the online version of this paper.**