Single-Use Device Reprocessing and Biocompatibility Testing

AMDR
ASSOCIATION OF MEDICAL DEVICE REPROCESSORS

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Amsterdam

Topics To Be Covered

- Introduction to AMDR
- Overview of commercial SUD reprocessing (remanufacturing)
- European regulations
- Biocompatibility testing
- Safety, savings, and sustainability

Introduction to AMDR

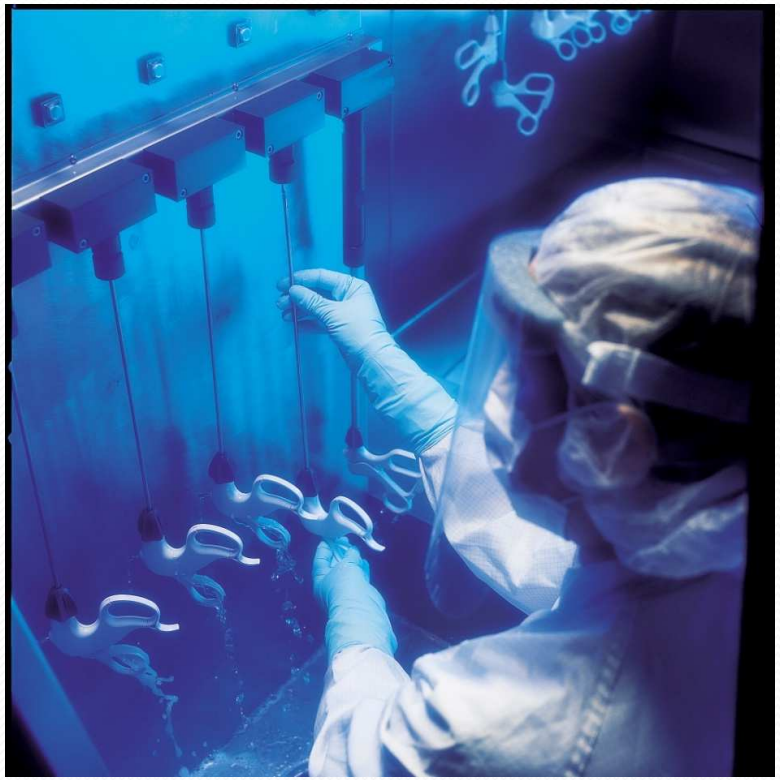
- International, non-profit, trade association formed in 1997 representing the legal, regulatory and other trade interests of commercial SUD reprocessors and remanufacturers

AMDR
ASSOCIATION OF MEDICAL DEVICE REPROCESSORS

- Members reprocess for a majority of U.S. hospitals and German academic medical centers plus over 1,000 European hospitals

Commercial Reprocessing Industry Since 2000

- Regulated as device manu-facturers since 2000 in U.S.
- Regulated and accepted under quality standards and validated procedures in Germany set by KRINKO since 2002
- Nearly $500 million industry today
- Serve every major hospital system in the U.S. and all the “honor roll hospitals”
- Serve 95% of German University medical centers
- Certified as Manufacturer for “fully refurbished medical devices” in accordance with EN ISO 13485 and the EU MDD 93/42/EWG



AMDR Member-Companies

- **Hygia Health Services**
  - Birmingham, Alabama
  - Focus on Non-Invasive Devices
- **Innovative Health**
  - Scottsdale, Arizona
  - Targeted, high-impact cardiology focus
- **Medline ReNewal**
  - Redmond, Oregon
  - Part of Medline Industries, largest privately held manufacturer and distributor of healthcare supplies in U.S
- **Stryker Sustainability Solutions, Inc.**
  - Tempe and Phoenix, AZ and Lakeland, FL
  - Division of Stryker Corporation since December 2009
- **Vanguard**
  - Berlin-Germany
  - European market leader

The "Single Use" Label and How OEMs Discourage Reprocessing

- Chosen by the manufacturer
- Not a regulatory requirement (in Canada, Europe or U.S.)
- Labels switched from "reusable" to "single-use" approximately two decades ago without structural changes for many devices
- Some devices sold as "reusable" in one country and "single-use" in another
- Some OEMs included "cleaning instructions" with SUDs
- Some OEMs had/have reprocessing programs

The "Single Use" Label

"The decision to label a device as single-use or reusable rests with the manufacturer. … Thus, a device may be labeled as single-use because …the manufacturer chooses not to conduct the studies needed to demonstrate that the device can be labeled as reusable."[1]

1 GAO, Report to the Committee on Oversight and Government Reform, House of Representatives; *Reprocessed Single-Use Medical Devices: FDA Oversight Has Increased, and Available Information Does Not Indicate That Use Presents an Elevated Health Risk* (January 2008), at 1 (emphasis added).

Emergence of Commercial Reprocessing

- Historically, most reprocessing was conducted in-house at the hospital
- The third-party reprocessing industry emerged in the U.S. and Germany approximately two decades ago in response to the growing cost of healthcare, including “single-use” devices and because third-parties can reprocess more effectively
- Globally, in-hospital reuse of SUDs is common

Safety Principles

- All commercially reprocessed devices meet cleaning/biocompatibility, performance and sterility specifications and requirements
- Complies with medical device manufacturer standards
- AMDR safety principles, include, among others:
  - 100% device testing and inspection
  - 100% device traceability
  - Commitment to reprocess only those devices that can safely be reprocessed

Commonly Reprocessed Devices

Commonly Reprocessed Devices

- **Arthroscopic/Orthopedic**
  - External fixation devices
  - Surgical saw blades, bits and burrs
- **Cardiovascular**
  - Sequential Compression Devices/Tourniquet cuffs
  - Pulse oximeter sensors
  - Femoral compression devices
  - Ultrasonic and electrophysiological diagnostic catheters
- **Non-Invasive Devices**
  - ECG leads
  - Air transfer mattresses
  - Blood pressure cuffs
  - Fall alarms
  - Pulse OX and cerebral and somatic sensors
- **Laparoscopic Surgery**
  - Trocars
  - Harmonic scalpels
  - Lap instruments: babcocks, dissectors, scissors/shears, graspers

Commonly Reprocessed Devices & Cost Savings

U.S. Dollars:

Ultrasound cardiac catheter:
- Cost new $2500 (each)
- Cost reprocessed $1250
- Savings $1250

EP diagnostic catheter:
- Cost new $400-600 (each)
- Cost reprocessed $200-300
- Savings $200-300

Harmonic scalpel:
- Cost new $250-500 (each)
- Cost reprocessed $125-250
- Savings $125-250

Euros:

Cardiac ablation catheter:
- Cost new 900-1500€ (each)
- Cost reprocessed 400-750€
- Savings 500-750€

EP diagnostic catheter:
- Cost new 300-500€ (each)
- Cost reprocessed 140-250€
- Savings 160-250€

Harmonic scalpel:
- Cost new 350-450€ (each)
- Cost reprocessed 180-220€
- Savings 170-230€

European Regulations

Current European Landscape

- Historically, no SUD reprocessing policy has existed at the European Union level
- Member States regulate on an individual basis
- SUD reprocessing likely occurring in hospitals across all Member States, regardless of national policy
- Regulated, third-party industry exists in Germany

Other Member States' Regulations

- Germany: Legal and regulated
- UK: in-house reprocessing discouraged, CE marked re-manufacturing allowed
- France: illegal
- Portugal: has strict guidelines which allow
- Most other Member States: no position
- Note: AMDR has evidence that the reuse of SUDs is common in Europe, even in countries where the practice is banned and/or discouraged

Current Situation is Unfair to Healthcare Professionals

- All devices, regardless of how labeled, should be safe and effective
- Arguably subjects patients to varying levels of safety
- Health professionals should not feel compelled into illicit reuse of "single-use" devices to save money
- Devices that can be reused should come with cleaning instructions from the manufacturer….
- OR hospitals should have the lawful ability to reuse medical devices by outsourcing to *regulated* third-parties that demonstrate safety/substantial equivalence with the manufacturer

European Regulations… Council/Parliament Version

- 17.1 – Where permitted by national law
- 17.2 SUD reprocessing is manufacturing
- 17.3 – MS may decide NOT to apply certain rules to reprocessing (for hospital and closed loop reprocessing) and outlines lengthy requirements
- 17.4- Reprocessing by service provider allowed
- 17.5 – Common specifications to be developed
- 17.6 – Only devices put on EU market
- 17.7 – Only safe reprocessing
- 17.8 – Reprocessor must label with their name

What does this mean?

- Unfortunately, not the harmonized approach AMDR had sought
- "Opt in" undermines the "single market"
- Stricter requirements for SUD reprocessors = higher regulatory burden than OEM devices
- MS "service" model:
  - Likely similar to existing German requirements
  - MDR requirements still exceed what hospitals can likely meet: Notified Body certification, reverse engineering, quality system, plus forthcoming common specifications, etc.
  - AMDR discourages other MS from allowing in-hospital, lesser regulated reprocessing

UK Policy

- Prohibits SUD reprocessing
- 2016 Guidance allows SUD remanufacturing
- Remanufactured SUDs must obtain CE mark
- Consistent with EU MDR - so “opting in”

Precedents

- US FDA –Full manufacturer requirements, 2000
- Supplemental validation data, 2004
- NB-MED Recommendation, 2.1/Rec5, *Placing on the Market of Fully Refurbished Medical Devices,* 2000
- Netherlands: RIVM, *Reprocessing of Medical Devices; Possibilities and Limiting Factors,* Arjan van Drongelen, 2008
  - Proposed that the reuse of SUDs should be defined as manufacturing
  - Required compliance with MDD including CE marking

Precedents

- UK: MHRA, *Single-use Medical Devices: UK guidance on Re-manufacturing*, 2015
  - SUD reprocessing (in-hospital): discouraged
  - SUD re-manufacturing (commercial, regulated) allowed and meet MDD (CE marking) requirements
- AMDR expects more Member States to "opt in" to the CE marking regulatory paradigm for SUD reprocessing

AMDR Position on EU-Regulation of Reprocessed SUDs

- Ensures doctors and nurses have consistent, safe and effective reprocessed or remanufactured SUDs
- Stops inappropriate hospital reuse
- Legitimizes commercial industry through EU-wide regulation
- Uses existing process of accreditation through notified bodies
- Encouraging Member States to “opt in” to CE marking paradigm

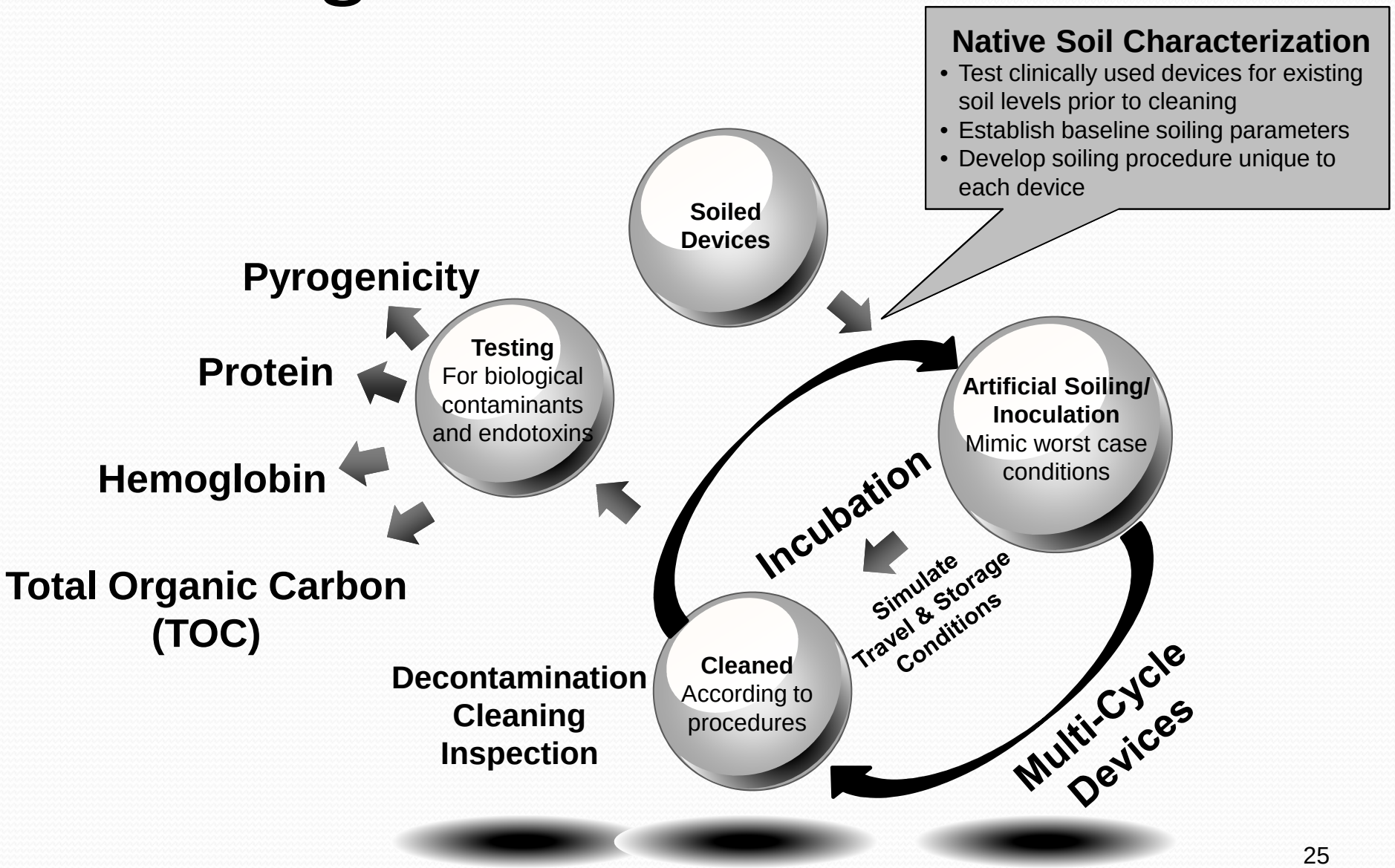
Reprocessing as Manufacturing

- Must meet all general obligations of manufacturers (Article 10)
- As part of this, SUD reprocessors/remanufacturers in particular must address:
  - Cleaning process validation
  - Biocompatibility
  - Performance
  - Sterility

Need for Notified Bodies & Consistent Policy

- Reprocessors/remanufactures CAN demonstrate compliance – let us show you
- Guidance needed –AMDR to work with Team-NB to provide common questions and answers and push uniformity in application of MDD/MDR requirements for SUD remanufacturers
- Guidance, examples:
  - Consistent labeling
  - Detecting OEM design changes
  - Understand OEM design/functional performance
  - Validation and biocompatibility requirements

Cleaning Process Validation



Design Control: Verify Biocompatibility

- Identify any biologic hazards the device has as a result of reprocessing.
- Biocompatibility testing follows the recommendations made in ANSI/AAMI/ISO 10993-1.
  - Categorization by nature of body contact and surface contact type
    - Non-contact device
    - Surface-contacting devices
    - External communicating devices
  - Categorization by duration of contact
    - Limited exposure: use likely ≤ 24h
    - Prolonged exposure: use likely > 24h, < 30 days
- Most common evaluation tests based on device types
  - Cytotoxicity
  - Sensitization
  - Irritation
- Devices are prepared under “worst-case” processing parameters (elevated temperatures, chemical concentration, exposure time); sterilized

Design Transfer: Cleaning Validations

- Product Inoculation
  - Simulated clinical use
  - Incubation of product (72 hrs. at 60° C)
- Annual Re-Validation of Cleaning Process
- Visible Contamination
  - Criteria must be established using visual aids
- Quantitative Cleaning Endpoints
  - Hemoglobin, Protein, Bioburden, Pyrogen, etc.

Design Transfer: Cleaning Validations

- Quantifiable Levels verified by product extractions (Laboratory Services)
- Equipment Qualification must be performed as pre-requisite
- Recommendations Found in References:
  - AAMI TIR No. 12 – 1994, Designing, Testing, and Labeling Reusable Medical Devices for Reprocessing in Health Care Facilities: A Guide for Device Manufacturers
  - AAMI / ANSI ST35:1996, Safe handling and biological decontamination of medical devices in health care facilities and in non-clinical settings
  - AAMI TIR 30, A Compendium of Processes, Materials, Test Methods, and Acceptance Criteria for Cleaning Reusable Medical Devices

Design Transfer: Performance Validations

- Worst-case Processing Conditions
  - Cleaning process parameters, clinical use, product inoculation, incubation, distribution simulation, thermal cycling (lowest to highest temperature extremes)
- Subsequent Device Testing
  - Function Testing using acceptance criteria derived from OEM benchmark testing.
- Equipment Qualification must be completed on equipment used as prerequisite

Safety

Regulated Reprocessing is Safe

- In-house (hospital) reprocessing has effectively been stopped in the US and Germany
- Nearly all SUD reprocessing conducted by regulated, third-party firms
- Very few adverse event reports
- 20+ years of clinical history
- Decades of peer-reviewed literature and clinical experience
- Support of major clinical

"we found no reason to question FDA's analysis indicating that no causative link has been established between reported injuries or deaths and reprocessed SUDs."

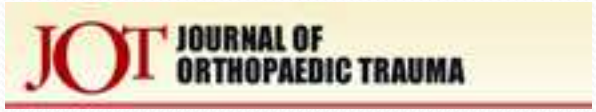
2008 US GAO Report, at 21-22.

"In January, after reviewing eight years of FDA data, the Government Accountability Office weighed in with a report concluding there is no evidence that reprocessed single-use devices create an elevated health risk for patients." –

THE WALL STREET JOURNAL

March 19, 2008, "Hospitals Reuse Medical Devices to Lower Costs."

Scientific Literature



Hospital & Clinical Community Support

AMERICAN NURSES ASSOCIATION

ENDORSED BY THE AMERICAN HOSPITAL ASSOCIATION

JOHNS HOPKINS MEDICINE
THE JOHNS HOPKINS HOSPITAL

AMERICAN COLLEGE of CARDIOLOGY FOUNDATION

AAOS
AMERICAN ACADEMY OF ORTHOPAEDIC SURGEONS

Top Hospitals

AMDR members serve all of the "**Honor roll**" **hospitals** recognized by *U.S. News & World Report*

- **Barnes-Jewish Hospital/Washington University**, St. Louis
- **Brigham and Women's Hospital, Boston**
- **Cedars-Sinai Medical Center**, Los Angeles
- **Cleveland Clinic**, Cleveland
- **Duke University Hospital**, Durham
- **Hospitals of the University of Pennsylvania - Penn Presbyterian**, Philadelphia
- **Houston Methodist Hospital**, Houston
- **Johns Hopkins Hospital**, Baltimore
- **Massachusetts General Hospital**, Boston
- **Mayo Clinic**, Rochester
- **Mount Sinai Hospital**, New York
- **Northwestern Memorial Hospital**, Chicago
- **NYU Langone Medical Center**, New York
- **New York-Presbyterian University Hospital of Columbia and Cornell**, New York
- **Stanford Health Care,** Stanford
- **UCLA Medical Center**, Los Angeles
- **UCSF Medical Center**, San Francisco
- **University of Colorado Hospital,** Aurora
- **University of Michigan Hospitals and Health Centers,** Ann Arbor
- **UPMC Presbyterian,** Pittsburgh

Financial

Economic Benefits

Reprocessing Provides a Multi-Fold Benefit to Hospitals:

- **Cost:** Immediate savings using the same brands physicians have always used
  - 50% cost savings, on average, for every reprocessed device utilized
  - Covers all third-party reprocessor costs: R&D, equipment and materials, staff, etc.
  - **Typical U.S. hospital could save around USD $0.5-2 million** per year

Economic Benefits

- **Disposal Cost Reduction:** Immediate reduction in red bag waste and associated disposal costs
- **Competition:** Hospitals that reprocess see reduced OEM pricing for new equipment and downward price pressure on other products
- **Moral high road:** Reprocessing allows hospitals to responsibly bend the cost curve, thereby extending their ability to do more with limited resources
  - Fiscally responsible
  - Environmentally sustainable

Sustainable Hospitals Help Bend the Cost Curve

"The savings achievable through sustainable interventions could exceed $5.4 billion over five years and $15 billion over 10 years."

-- Research from Commonwealth Fund, with support from Health Care Without Harm and Robert Wood Johnson Foundation

- Hospitals' cost savings by contracting with an FDA-regulated medical device reprocessor:
  - Over five years was about $57 per procedure. If adopted nationwide, cost savings would be $540 million annually, or $2.7 billion over five years."
    - Does not require any up-front hospital capital investment to get started
    - Same standard of care
    - Extend the life and value of the medical devices *already own*.

Environmental

Environmental Benefits

- Reprocessed SUDs are the single most impactful sustainability initiative currently undertaken by US hospitals
- American Nursing Association, Association of periOperative Registered Nurses, Practice Greenhealth and Health Care Without Harm have all recognized or endorsed reprocessing as a way to reduce waste
- Titanium, gold, platinum, steel and valuable plastics recovered/recycled instead of disposed
- Identified as a Smarter Purchasing initiative of the Healthier Hospitals Initiative (HHI)

Hospital Waste Reduction

- On average, **hospitals can reduce annual medical waste by 50,000 pounds.** This is the equivalent weight of more than 5 elephants.

- Titanium, gold, platinum, steel and valuable plastics can be recovered/ recycled instead of thrown away.

Summary

- Regulated SUD remanufacturing:
  - Promotes patient safety/public health
  - Reduces healthcare costs
  - Promotes competition
  - Protects the environment
  - Levels regulatory playing field
- SUD remanufacturing is coming
- AMDR expects most of Europe will opt IN to the CE marking paradigm

Thank You

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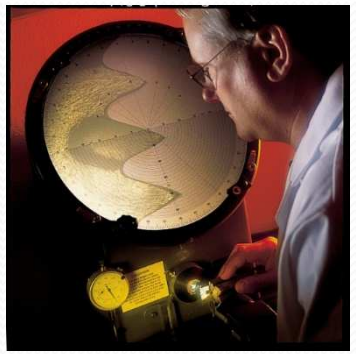
Developing a Reuse Procedure

Premarket research:

- Reverse engineering
- Destructive testing
- Biocompatibility
- Cleaning and process validation
- Endotoxin analysis
- Function testing parameters



Design Inputs: Validating a Device for Reuse

- Is the device similar to others currently reprocessed
  - Evaluate materials of construction
  - Research sterilization methods
  - Evaluate packaging concerns
  - Identify performance characteristics
  - Identify packaging configuration

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Validating Devices for Reuse

- Native Soil Characterization
  - Test clinically used devices for existing soil levels prior to cleaning.
  - Establish baseline soiling parameters.
  - Develop soiling (inoculation) procedure unique to each device.
  - Evaluation of “native” devices and assessment of qualitative (visual) and quantitative (extractions for protein, Hb, bioburden, etc.) contamination.

Design Control: Analyzing Functional Performance

- Performance:
  - Reverse Engineering - The process of analyzing a medical device to identify its critical components and their interrelationships in order to better understand function and establish performance specifications
  - OEM Benchmarking – Defining and establishing functional substantial equivalence.
    - Establish pass/fail criteria
    - Mechanical and electrical properties
    - Penetration, Grasping, Cutting Forces

Design Control: Building Device Profile

- Disassembly / Reassembly Methodology
  - Customized fixtures for device disassembly and reassembly, where applicable
- Drawings
  - Product geometry / Surface area calculations
  - Testing fixtures
  - Replacement parts
- Goals:
  - Establish tolerance/dimensions
  - Fixture integration
  - Internal components

Design Control: Process Development

- Cleaning Process Development
  - Chemical identification
  - Process parameters (dwell time, temperature, chemical concentration)
  - Customized cleaning fixtures
- In-line Visual Inspection
  - Cleaning efficacy
  - Proper assembly
  - Structural integrity

Design Control: Process Development

- Performance
  - In-line Function Testing
    - Development of most appropriate in-line functional testing to produce safe and effective product.
      - Electrical Testing
      - Insulation Testing
      - Dye Penetration Testing (Ultrasonic Scalpels)
      - Cannula-Seal Leak Testing (Trocars)
  - Packaging & Labeling
    - Development of most appropriate packaging to produce safe and effective product to the customer.
    - Development of labeling that is substantially equivalent to OEM labeling.

Design Transfer: Validations

- Validation of Processes
  - Cleaning, Performance (Functionality), Packaging
- Evaluation of Worst-Case Processing Parameters
- Reference:
  - Guideline on General Principles of Process Validation, May 1987 – U.S. Food and Drug Administration, Center for Drug Evaluation and Research

Design Transfer: Sterilization Evaluations

- Ethylene Oxide Residual Evaluation
  - Ensure materials of construction (after reprocessing) are able to properly aerate gas under normal aeration times (ISO 10993-7)
  - Samples are prepared at nominal (routine) conditions
  - Sent to external laboratory (on dry ice)
- Comparative Resistance
  - Purpose: Demonstrate that the test device does not pose a greater sterilization challenge than the PCD used in the validation of the sterilization process.
  - Identify most challenging locations for sterilization for inoculation.
  - Exposed to EO sterilization parameters (with PCD used in validation) to identify which device is more difficult to sterilize
- Annual Sterilization Validations

Design Transfer: Packaging & Stability Validations

- Worst-case Processing Conditions
  - Distribution Simulation
  - Thermal Cycling
  - Ageing (Accelerated & Real-Time)
- Pouch
  - Tensile Strength Testing
  - Dye Penetration Testing
- Subsequent Performance Verification of device functionality

Summary

- No hazards in terms of
  - Infections
  - Reactions as a result of pyrogene
  - Allergic reactions
  - Toxic reactions
  - Change of technical-functional features

- Technical-functional safety regarding to
  - Surface
  - Corrosion
  - Embrittlement
  - Tensile strength; breaking strenght
  - Stability of bonding/contact points
  - Lubrication
  - Residues of process chemicals
  - Integrity of case parts

- Function test (product-specific standards e.g. ISO 60601)

Summary

- Specific to the Device
  - EP Catheters:
    - Electrical Tests: Resistance, continuity, di-electric leak
    - Mechanical Tests: Pull / torque tests, deflection, steerability
    - DEPCTS
  - Ultrasound Catheters
    - HIPOT, FirstCall, Image Testing, Deflection
  - Shaver Blades:
    - Drop test, Free Rotation Tests, Visual Standards
  - Soft Tissue Ablation:
    - Electrical Tests: Continuity
    - Mechanical Tests: Electrode measurement
  - Laparoscopic Scissors:
    - ASTM latex cut test, current leakage
  - Compression Sleeves:
    - Inflation test, Leak decay
  - Trocars
    - Seal tests, Burst pressure testing
  - Harmonic Scalpels
    - Console check, Spring force constant, Blade temperature, thermal spread
  - External Fixation
    - Stress, fatigue, range of motion, static/dynamic tests
  - Sealer / Dividers
    - Electrical: Thermal Spread, Max Tip Temp, Cooling Time, Burst Pressure, EMC and Electrical Safety
    - Mechanical: Handle Lock/Unlock, Jaw Close, Jaw Open, Cutting Trigger Actuation, Jaw Clamp Force

Summary

Japanese noted differences:

- **Use of Re-Engineering to Prove Substantial Equivalence**
- **Use of Re-Engineering to Provide Materials Data**
- **Specification of Reprocessing Design Requirements**
- **Description of Re-manufacturing Process instead of Manufacturing Process**
- **Re-Manufacturing Process Validation, Including Additional Functional Testing**
- **Stated Number and Evidence Regarding Maximum Number of Cycle Times**
- **Native Device Testing**
- **Description of Cleaning Process**
- **Cleaning Process Validation**
- **Augmented Risk Assessment to Account for Re-manufacturing Risks**
- **Replacement Parts / Components Description and Material**
- **Modifications to Labeling and Tracking Procedures**
- **Assessment of OEM Design Changes**

- From Japan MHLW Re-Manufacturing Study Mission, March, 2016