The Future of Radiation Sterilization - The Perspective of a Contract Service Provider

KATHY HOFFMAN AND KEVIN O’HARA
2018 CIRMS MEETING

APRIL 2018
CONFIDENTIAL
Scope

• A brief overview of the healthcare industry today, and the pace of technology advancement.

• Increasing complexities of the radiation-processing world due to technology advancement.
  • The need for the radiation-processing industry to find ways to minimize radiation damage, develop new approaches, partner with the device manufacturer in an increasingly complicated regulatory environment.

• iiA 2017 Publication
  • A Comparison of Gamma, E-beam, X-ray and Ethylene Oxide Technologies for the Sterilization of Medical Devices and other Products.

• Discussion
New Publication

- A Comparison of Gamma, E-beam, X-ray and Ethylene Oxide Technologies for the Sterilization of Medical Devices and other Products
  - Published by the iiA in 2017
  - www.iiaglobal.com
  - Brief overview in today’s presentation

A Comparison of Gamma, E-beam, X-ray and Ethylene Oxide Technologies for the Industrial Sterilization of Medical Devices and Healthcare Products

AUGUST 31, 2017
Sotera Health

Nelson Labs
A Sotera Health company

- Pre-FDA Validation & Quality Control testing of the stent, pacemaker, vaccine & syringe, protective gowns/masks, and all IV tubes
- Creates the cleaning protocols for medical equipment used in operating room procedures

Nordion
A Sotera Health company

- Radioisotopes used for diagnostic imaging, Gamma rays for Gamma Knife treatment used on brain tumors

Sterigenics
A Sotera Health company

- Conducts the sterilization process & post sterilization validation of the stent, pacemaker, drapes, gowns, masks, tubing, syringe & vaccine and bandages
The convergence of technologies has and will continue to drive the development of ever-more complex sterile health care products.

Treatment of symptoms → Cure

But, with much more emphasis on prevention.

To succeed in this environment the radiation processing industry must:

- Discover techniques to minimize radiation damage to bioactives and fragile molecules
- Develop specialized equipment
- Partner with a diverse group of health care product developers
- Function in a more complex regulatory environment

(Liu, 2007)
Worldwide Medical Technology R&D Spending

R&D Spending as a Percentage of Sales Revenue.  
Source: Statistica.com 2018
Med. Technology R&D Spending by Company

R&D Spending in 2015; projected for 2022.  Source: Statistica.com 2018
Advancements in Science and Technology Have Made Innovations Possible

Foundational Engineering (Mechanical, Electrical, and Chemical)

Material Science

Polymer Chemistry

Pharmacology

Advanced Imaging

Data Processing

Breakthrough Innovations

John M. Capek, Executive VP
Abbott Ventures
IMRP, Vancouver, 2016
Complexity of Medical Device Evaluations

Cytotoxicity
- assess interaction of medical device or extract with mammalian cells.

Sensitization
- estimate the potential for contact sensitization by medical device or extract.

Irritation
- measures the irritation potential of the medical device or extract.

Systemic Toxicity
- assesses the toxicity potential of the leachables and degradation products upon single or multiple exposures.

Genotoxicity
- assessing potential to cause a mutation which could lead to a tumor.

Implantation
- gross and microscopic examination of a device in contact with bone or tissue.

Leachability, Extractability testing.....
Increased Regulatory Environment.....
The use of temperature sensitive bio-resorbable polymers for timed release of active agents continue to emerge, including devices that utilize active electronics.

Common to all of these medical product sectors with their sensitive materials is the need for safe, robust, cost-effective sterilization.

Source: Abbott Vascular
Some Trends in Health Care

• Growth in single-use combination type drug, biological, electronic and device products.

• Drug eluting stents which carry multiple drugs, including infection control, pain control, and regenerative medicines.

• Successful irradiation of combination products requires fresh thinking.

• Products likely have an extremely low bio-burden, and a resulting tight dose tolerance.
Novel Sterilization Approaches

• If EO and radiation are incompatible with a combination device, utilization of novel technologies may be a path forward.....

  – If oxidizing agents like hydrogen peroxide, ozone, and chlorine dioxide are compatible with product materials, these modalities have the benefit of processing close to room temperature.

  – Nitrogen dioxide sterilization is being developed; its mode of kill and material degradation is nitration so it may offer promise for additional materials.
Novel Sterilization Approaches

• If EO and radiation are incompatible with a combination device, utilization of novel technologies may be a path forward.....
  – Alternatives are not high-volume technologies, and may be expensive. BUT they may be less expensive and provide higher patient safety profile than aseptic processing.

• Other possibilities:
  – Peracetic Acid Vapor Dry Heat
  – Hydrogen Peroxide
  – Peracetic Acid Vapor

• Newer technologies, smaller volume processing, but may offer the best alternative for a new device...
Challenges for Aseptic Processing

• Validation of process
  – Sterilization of processing equipment
  – Controlled access to aseptic area
  – Measurement of Sterility Assurance Level (SAL)
  – Costly process and potentially risky

• FDA: Seek terminal sterilization wherever possible

• BUT...Aseptic manufacturing is an accepted and established method.
Terminal Sterilization Benefits

• Benefits of EO and radiation are well established....

• Low Cost of Evaluation During Developmental Process.

• Potential Sterilization Cost Savings.

• Ease of Process Validation to a Sterility Assurance Level of $10^{-6}$. 
Terminal Sterilization & Pharma: Challenges

• Radiation easy to validate but has challenges
  – Must be decided in “Discovery” stage of pharmaceutical life cycle
    • Scientists/Engineers must be aware of the impact on sterilization
  – Time from fill to terminal sterilization is critical
    • Some Pharma products may support microbial growth
  – Extremely low doses required for most products
    • Straightforward in practice, difficult for some large-scale facilities
  – High processing temperatures may impact the API
  – Radiation compatibility of the API needs to be assessed
The Future is Here

- Increasing product & process complexity
- Requirement to protect bio-actives
- Free radical scavengers
- Low temperature irradiation
- Need for non-traditional approaches to sterilization
- Aggressive development time lines for introducing new products
- Bio-absorbable materials less tolerant to sterilization than metallic counterparts
Mitigation of Radiation Challenges

- Utilize Specialized Equipment to provide unique irradiation capability to deliver precise and low doses.
- Expedited services provide capability to irradiate product immediately to prevent micro growth.
- Use modified environments for the irradiation of unstable products.
- Use Sterilization Scientists with extensive years of experience developing sterilization methods.
New Publication

- Descriptions of each technology
- Modality Comparison
  - Suitability
  - Equipment
  - Economics
  - Environment
- Every attempt to ensure impartiality
- WP is available at www.iiaglobal.com

A Comparison of Gamma, E-beam, X-ray and Ethylene Oxide Technologies for the Industrial Sterilization of Medical Devices and Healthcare Products

AUGUST 31, 2017
New WP – Comparison of Technologies

TABLE 1: FACTS AT-A-GLANCE

- **Global Sterilization Market**
  - **Actual Value**: US $4.69B in 2016
  - **Forecasted Value**: US $6.93B in 2021

Source: MarketsandMarkets, December 2016

- **Breakdown of the Sterilization Market**
  - 40% gamma
  - 50% EO gas
  - 4.5% e-beam
  - 5% other

Sterilization market is dominated by North America, followed by Europe, then Asia, then rest of world.

Source: MarketsandMarkets, December 2016

- **'Offsite' or 'Contract' Sterilization Market**
  - Accounts for the largest share of the market in 2016

Source: Medical Design and Outsourcing, August 2016

- **Value of US Medical Device Market in 2015**: US $140B
- **US Market Share of Global Medical Device Market in 2015**: 45%
- **Value of US Exports of Medical Devices in 2015**: US $45B

Source: International Trade Administration, May 2016
Summary

• Technology & Innovation will continue to be A Key Force in Healthcare.

• Effective radiation sterilization of combination products and pharmaceuticals are happening today.
  – The selection of the irradiation conditions needed to help maintain its functional properties.
  – Customized solutions (modified atmospheres).
  – Effective radiation sterilization techniques provide a safe and effective drug/product.
  – New methods for establishing a sterilisation dose to minimise radiation damage of the product.
  – Careful evaluation of alternative sterilization techniques
Human Tissues and Biologics

Chronology of Tissue Irradiation

– Past
  • Initial studies in 1950s and 1960s
  • Standard processing techniques
  • Outcome – Poor mechanical results

– Recent: 5 to 10 Years
  • Reducing the minimum dose requirements
  • Control Environmental conditions during irradiation (and pre/post) and/or use radio-protectants
Human Tissues and Biologics

- Lower temperature irradiations used to minimize mechanical degradation
- Dry ice irradiations to Low temp chamber
Technology Convergence in Medical Devices
Technology & Innovation: A Key Force in Healthcare

Source: JnJ IMRP Conference

1890s to 1950s
- Aspirin
- Penicillin
- Sterile wound care products
  - First flu vaccine
  - Polio vaccine
  - X-ray
  - Pacemaker

1960s to 1970s
- Valium
- Haldol
- Open heart surgery
- Beta blockers
- MRI invented
- Hip replacement

1980s to 1990s
- Biologics (e.g., mABs, TPA, Epo)
- Statins
- Anti-psychotics
- Stents
- Defibrillators
- Angioplasty
- Minimally invasive surgery

2000s and beyond
- Drug coated stents
- Genomics and proteomics
- Targeted therapeutics
- Molecular diagnostics
- Gene therapy
- Stem cell repair
  - Health management
  - Evidence based medicine
  - Self pay products/services

J&J Innovations
Business model/customer innovation
Technology Advancements Drive Next-Generation Integrations

- Structural Materials
- Nano Technology
- Genomics
- Imaging Modulation
- Artificial Intelligence
- Telemedicine
- Antimicrobial Materials
- Tissue Engineering

Heart Diseases
Cancer
Diabetes
Respiratory
Neuro Disorders

John M. Capek, Executive VP
Abbott Ventures
IMRP, Vancouver, 2016
## Challenges to Technology Innovation

<table>
<thead>
<tr>
<th>Challenge</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost Pressures</td>
<td>Government restrictions and shift to consumers</td>
</tr>
<tr>
<td>Globalization</td>
<td>Adoption of reference-based pricing (establish baseline product that all competitors are reimbursed against)</td>
</tr>
<tr>
<td>Patent/IP Law</td>
<td>Emerging market intellectual protection laws</td>
</tr>
<tr>
<td>Premium Reimbursement</td>
<td>Health economics and cost effectiveness required beyond efficacy and safety</td>
</tr>
</tbody>
</table>

---

John M. Capek, Executive VP  
Abbott Ventures  
IMRP, Vancouver, 2016
Pillars of Public Health

- Pasteurization
- Immunization
- Chlorination
- Food Irradiation

Who Supports Food Irradiation?

- World Health Organization
- Canadian Medical Association
- American Medical Association
- Centers For Disease Control (CDC)
- American Dietetic Association
- Institute of Food Technologists
- American Council on Science and Health
- U.S. Food and Drug Administration
- American Public Health Association
- United Nations

Source: Dr. Michael Osterholm
Gamma Sterilization Of Pharmaceuticals

—Case Studies:

• Human Tissues & Biologics
• Bone Grafts
• Virus Inactivation