H$_2$O$_2$ Industrial Sterilization

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Agenda

• H$_2$O$_2$ Sterilization Technology
  • Typical H$_2$O$_2$ sterilization cycle
  • Gas vs liquid state
• Material compatibility
• Industrial Application
• Conclusion
Generic H$_2$O$_2$ Sterilization Cycle

Sterilization phases, repeated 1 to 3 times

- Vacuum
- H$_2$O$_2$ injection and dwell
- Air or O$_3$ injection and dwell
- Ventilation/ aeration

Pressure vs. Time Graph

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**H₂O₂ Sterilization Technology - Sterilant**

**Sterilant:** H₂O₂ solution

- 50 to 59% (w/w)
- Stabilizing agent(s) to improved shelf-life
- Liquid at normal temperature and atmospheric pressure
- **Boiling point:**
  - Water: 100ºC
  - H₂O₂: 150.2ºC

**Sterilizing agent**

- H₂O₂/H₂O is vaporized to form the sterilizing agent (VH₂O₂)
- Using heat and low pressure (similar to water)

**VH₂O₂**

- Sterilize in gas and liquid form
- Physical state: depend on temperature and pressure
- Predicted by Isotherm diagram

![Isotherm Diagram](image)

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**Working zone of a low temperature sterilization process**
Micro-condensation of a 50% H₂O₂ solution with a load at 26 °C

In practice

Dew pressure for 50% H₂O₂ at 26 °C

What is micro-condensation?
# Impact of temperature

Dew pressure (Torr) for different temperature

<table>
<thead>
<tr>
<th>Temperature</th>
<th>0% $\text{H}_2\text{O}_2$ (100% water)</th>
<th>50% $\text{H}_2\text{O}_2$</th>
<th>59% $\text{H}_2\text{O}_2$</th>
<th>100% $\text{H}_2\text{O}_2$</th>
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<tbody>
<tr>
<td>10</td>
<td>9.2</td>
<td>1.6</td>
<td>1.4</td>
<td>0.6</td>
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<td>3.5</td>
<td>2.9</td>
<td>1.4</td>
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<td>50</td>
<td>92.6</td>
<td>23.8</td>
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<td>10.0</td>
</tr>
</tbody>
</table>

$\text{H}_2\text{O}_2$ is condensing first.
Vapor process doesn’t mean 100% vapor

Hydrogen peroxide needs to stay in gas state long enough to penetrate packaging and reach the device to be sterilized
Material compatibility

- VH2O2 is an oxidizing process
  - May oxidize organic material or non-oxidizing resistant materials
    - Butyl, Natal rubber, silver, bioabsorbable, cellulose
  - Compatibility for 1-2 cycles is good for most material
    - See AAMI TIR 17 Annex E (H₂O₂) and I (H₂O₂ +O₃)
    - May be different if plasma or ozone are part of the process
      - Plasma: limited compatibility with Polyacrylate
      - Ozone: EPDM (grade-dependent)
  - Specific metals (e.g. iron, copper, platinum) catalyze the decomposition of H₂O₂
  - Number of cycle minimum for industrial sterilization (1 or 2 cycles), thus less impact on adhesive

∴ Most materials are compatible
Material compatibility - Packaging

• VH2O2 cannot penetrate through non-porous material
  • Packaging used need to have a porous membrane
  • Not compatible with aluminium pouch

• VH2O2 will be adsorbed by cellulosic material ⇒ failed cycles
  • Not compatible with paper pouch
  • Not compatible with cardboard boxes

• VH2O2 compatible with:
  • high-density polyethylene (HDPE) membrane such as Tyvek®
Material compatibility – Residual $\text{H}_2\text{O}_2$

- $\text{H}_2\text{O}_2$ is adsorbed by porous material
  - Ex: Polyurethane, polyester, polyoxymethacrylate, polysulfone
- $\text{H}_2\text{O}_2$ residues causes cytotoxicity at a very low level (around 0.001%)
  - Positive cytotoxicity ≠ in vivo reaction
- $\text{H}_2\text{O}_2$ residual concentration will decrease over time
  - $\text{H}_2\text{O}_2$ half-life in air: 10-20 hours
  - Will be below the cytotoxic level before the use of the medical device

∴ Residual $\text{H}_2\text{O}_2$ is not an issue if materials are compatible
**H₂O₂ Industrial Application – Current use**

- Low volume, high-margin devices such as custom made implants (3D print)

- Exterior sterilization of single-packaged vials (injectable drug), pre-filled syringe assembly

(Juha Mattila. 2014. STERIS VHP Low Temperature Surfaces Sterilization: Product feasibility testing, cycle development and validation guidance)

**H$_2$O$_2$ Industrial Application - Limitations**

**Non-linear inactivation**

![Graph showing non-linear inactivation](image)

**Loading Capacity: claims**

- Hospital based sterilizers not designed for high volume product
- Limited weight per load: depend on device material (porous or not)
- Load conditioning: temperature of load will affect the physical state of the vaporized H$_2$O$_2$

**Lumen claims**

- Based on type (rigid vs flexible) and material (Teflon vs silicone or other polymer)
- Quantity per load
- Currently: no claims for single-use catheter type devices

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**Liquid**

- **Open**
- **Vacuum resistant**

Can hydrogen peroxide sterilization serve as an alternative for industrial EtO sterilization of medical devices in the short or long term?

**YES:** for many specific devices, mostly surface devices package using a permeable membrane such as Tyvek®

**PROBABLY NOT:** for flexible lumens with ID < 0.7 mm