The Removal and Inactivation of Prions

December 6th to 8th, 2007
Bydgoszcz, Poland
Peter Newson
Marketing Manager -EMEA
Agenda

1. Introduction
   1. Subject
   2. Risks
   3. Standards

1. Prion introduction

3. Cleaning
   1. Decontamination
   2. Prion inactivation
Target

Inactivation of prions on infectious proteins
The subject

- Contaminated surgical instruments need to be cleaned to remove soil and infectious items and proteins
Soil-A Dirty Subject

• Implications of inefficient cleaning
  – Visually unacceptable devices
  – Ineffective disinfection and sterilization
  – Device damage
  – Adverse patient outcomes
  – Accidental prion transmission
Increased Attention

- Visually unacceptable devices
  - Cancelled procedures
- Device damage
  - Dried on soil / salt deposits
- End toxins
- TASS
  - Toxic Anterior Segment Syndrome
  - Outbreak in the USA
  - Cataract surgery
  - Inadequate cleaning and/or water residuals
What has Changed since 2000?

- The Science of cleaning
- Understanding of “Prions”
- Revolution in Prion Decontamination
  - New Investigations
  - New products

- New Regulatory Focus
What has changed......

......and reasons for the development of new and more effective decontamination methods:

- Patient risks
- New Standards
- Increased attention
Patient risks

- Inadequate disinfection and sterilization
- Toxin risks
- Prion diseases
  - Other protein disease concerns
Standards for decontamination

- EN/ISO 15883 series
  - Published
    - Part 1: General requirements, definitions and tests
    - Part 2: Requirements and tests for washer-disinfectors employing thermal disinfection for surgical instruments, anaesthetic equipment, hollowware, utensils, glassware, etc.
    - Part 3: Requirements and tests for washer-disinfectors employing thermal disinfection for human waste containers
  - In final draft (FDIS)
    - Part 4: Requirements and tests for washer-disinfectors employing chemical disinfection for thermo-labile endoscopes
  - Technical Specification (TS)
    - Part 5: Test soils and methods for demonstrating cleaning efficacy of washer-disinfectors
Standards for sterilization

- EN/ISO 17665, *Sterilization of medical devices* - *Information to be provided by the manufacturer for the processing of resterilizable medical devices*

- Others
  - Biocides directive (98/8/EC; April, 1998)
  - REACH (Com(03) 644)
    - ‘Registration Evaluation and Authorisation of Chemicals’
Prion introduction

• What are ‘Prions’?
  – Identified as the causative agents for a group of central nervous system diseases
    • TSEs (Transmissible Spongiform Encephalopathies)
    • vCJD, CJD (Creuzfeldt-Jacob disease)
  – Still debated!
    • Proteins
    • Appear to be devoid of nucleic acid
Prions and protein folding: The cause of vCJD appears to be the presence of an abnormal forms of normal protein, known as a **prion**. This structure makes them hard to be removed from the instruments.

- Accumulate in the body and Causing cell death (brain).
- No more cell growth
Prion decontamination

- Intrinsic resistance
  - Prions demonstrate resistance to routine methods of decontamination and sterilization
  - Prions are proteins, not microorganisms

Enveloped Lipid Viruses (HIV)
Large Non-Enveloped Viruses
- Vegetable Bacteria
- Fungi
- Non-Enveloped Lipid Viruses
- Mycobacteria
- Bacteria Spores

PRIONS?
Accidental transmission in practice

Source of CJD

Patient (female)
Age: 69
Exposure Sept. 1974

Case 1

Patient (female)
Age: 23
Exposure Nov. 1974
Death 20 month later

Case 2

Patient (male)
Age: 17
Exposure Dec. 1974
Death 16 month later

Implantation

Chimpanzee
Age: 17
Exposure Dec. 1977
Death 20 month later

Assay

1-2 new diseases per 1 Mio. People a Year / Global
STERIS Research Facility

• Fontenay-aux-Roses, Paris
  – Laboratory facilities
    • Microbiology (Biosafety 1-3), histology and biochemical laboratories
  – Atypical pathogen research
    • Including Prions

*In Vivo* and *In vitro* sets where carried out in collaboration with STERIS
The science around cleaning

• The chemistry of soil
• How much and what is present
• Detection of soil
• Cleaning indicators
• ‘New’ cleaning methods

• ….How clean is clean?
Concerns with cleaning

- Infectivity is difficult to remove from instrument surfaces
- Drying of soil increases risk
- Improper handling increases risk
- Some standard cleaning processes may also increase risk
- Impractical recommendations
Considerations

- **Efficacy**
  - Data is conflicting
  - Testing on surfaces

- **Compatibility**
  - Surface damage

- **Safety**
  - Handling

**WHO process:** Emerge instruments in a High concentration of Sodium Hydroxide
Where should reprocessing begin?

• Point of use (OR)

• WHO, NICE, AORN Guidelines recommend instruments should not be allowed to dry

Instrument transportation gel / pre-soak
Important Detergent Concepts

- **Regulations**
  - Claims

- **Safety**

- **Process**
  - Contact Method, Time, Temperature, Concentration
  - Water quality

- **Formulation**
  - A combination of ingredients, including active and inert ingredients, into a product for its intended use
New Cleaning Technology

- Enzymatic formulations
  - Genencor
  - Alkaline proteases
  - Effect of formulation
- Advances in alkaline cleaning
- Physico-chemical cleaning
  - e.g., plasma
### Cleaning performance

- Cleaning performance test on static emulsion

<table>
<thead>
<tr>
<th>Enzymatic Methods</th>
<th>&quot;Log&quot; Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Klenzyme</td>
<td>~4.5</td>
</tr>
<tr>
<td>Enzyme Cleaner 2</td>
<td>~1</td>
</tr>
<tr>
<td>Porous load autoclaving 15 min at 121°C</td>
<td>~5.5</td>
</tr>
<tr>
<td>Klenzyme + autoclaving</td>
<td>~6.5</td>
</tr>
<tr>
<td>Enzyme Cleaner 2 + autoclaving</td>
<td>~3.0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Alkaline Methods</th>
<th>&quot;Log&quot; Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hamo50 (1%, 65°C; 10 min.)</td>
<td>~3</td>
</tr>
<tr>
<td>Hamo50 (1%, 70°C; 10 min.)</td>
<td>~6.5</td>
</tr>
<tr>
<td>CIP150 (1.6%, 43°C; 15 min.)</td>
<td>&gt;7</td>
</tr>
<tr>
<td>Hamo100 (1%, 65°C; 10 min.) (0.8%; 43°C; 7.7 min.)</td>
<td>&gt;7</td>
</tr>
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Not all enzymatic & alkaline cleaners perform in the same way.

Detergent formulations are critical for prion inactivation & removal.
Two in one Detergent

- Outstanding Cleaner
- Removes and Inactivates Prions
Key product components

- Potassium Hydroxide (KOH)
- Surfactants
- Chelating Agents
Why Potassium Hydroxide (KOH) over Sodium Hydroxide (NaOH)?

- Both increase the solubility of soils
- Potassium ions and salts are more soluble in water than Sodium ions and salts
- No need to neutralize with acid

- Better Rinsing Ability!
Key product components

- **Surfactants- Surface Active Agent**
  - Penetrate soil and surface irregularities
  - Ability to displace particles

No Surfactants  Surfactant A  Surfactant B
Key product components

Chelating Agents

- Sequester hard water ions
- Keeps them in a suspension
- Prevents them re-depositing on surface
Prion Decontamination Cycle

- **Manual Soak with HAMO100 PID**
  
  - Fill basin with water to a temp of 43°C (keep warm)
  - Add 0.8% Hamo 100 PID
  - Submerge instruments in water (5cm above instruments)
  - Typical soak time = 7.5 min
  - Rinse and then pass through normal process
### Prion Decontamination Cycle

- **HAMO 100 PID usage in washer/disinfector**

<table>
<thead>
<tr>
<th>Phase</th>
<th>Temp</th>
<th>Time</th>
<th>Concentration</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-Wash</td>
<td>≤ 43 °C</td>
<td>1 – 2.5 min</td>
<td>0.2%</td>
<td>Dosed pre-wash can be used when instruments have been allowed to dry</td>
</tr>
<tr>
<td>Wash</td>
<td>≥ 43 °C</td>
<td>4 – 7.5 min</td>
<td>0.2 – 0.8%</td>
<td>Concentration depends on water quality</td>
</tr>
</tbody>
</table>
How does the formulation act

- **Removes** prions & bioburden from surfaces
- Keeps them **suspended**
- **Inactivates** through **hydrolysis** & allows suspended residues to be **freely rinsed** without re-adhering to the surface
- **Substrate Compatibility** (Instrument materials)
Hydrolysis as inactivating mechanism

• Breaks down the peptide bonds through the introduction of water between the atoms of the bond, thus inactivating the infectivity of the prion
Degradation with Hamo 100

- >6 log reduction in prion titers against multiple strains of prions including CJD & vCJD
- Total cleaning of ISOEN15883 part 5 test soils incl. Edinburgh & blood soils
Degradation with Hamo 100

<table>
<thead>
<tr>
<th>Exposure Time</th>
<th>Unexposed controls</th>
<th>% Hamo100</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 mins</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7 mins</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>263K</th>
<th>6PB1</th>
<th>BSE</th>
<th>sCJD</th>
<th>vCJD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alkaline Cleaner 43°C</td>
<td>0.8%</td>
<td>1.6%</td>
<td>0.8%</td>
<td>1.6%</td>
<td>0.8%</td>
</tr>
<tr>
<td>Control</td>
<td></td>
<td></td>
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Conclusion

- Prions can be transmitted on device surfaces
- Methods have been developed to verify the effectiveness of decontamination methods
- Cleaning alone can be effective
  - Choice of cleaner and process is important
- Disinfection and sterilisation can be effective
  - Choice of biocide and process is important
  - New methods of prion decontamination have been identified