Personnel Exposure to Isoflurane Before and After Placement of Accessory Anesthesia System

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New Technology

- Xenogen IVIS (In Vitro Imaging System)
  - Non-invasive
  - Biophotonic imaging
  - In Vitro
Firefly Power

- Firefly’s luc gene
- Luciferase production
- Luciferin + Luciferase = GLOW
“Nude” Mice

- These Immune-compromised mice can have human tumor tissue (with the spliced luc gene) implanted into or onto them.
Let It Glow

- Luciferin injection
- Luciferase Producing Tumor cell

Luciferin + Luciferin = GLOW
Cooled CCD camera
Light Sealed Box
Imaging Stage
Mouse
Say Cheese

- Imperative to chemically restrain
- Isoflurane
  - halogenated anesthetic
  - induce and maintain anesthesia
Experimental Procedure

- *Fill vaporizer with isoflurane*
- Add mice to induction chamber
- Turn vaporizer on
- Wait for mice to be anesthetized
- Switch anesthesia tubing from induction chamber to Xenogen camera box
- *Open induction chamber and remove mice, close lid to chamber*
The Camera Box

- *Position mice in Xenogen camera box*
- Delicate process
Next Steps

- Inject luciferin
- Close camera box
- Mice are imaged using camera and computer
Last Steps

- Anesthesia switch
- Oxygen flush
- Open camera box door
- Mice are removed to cages for recovery*
First Sampling Results

- Staff that had been using equipment most complained of headaches
- Vaporizer
- 20 minute imaging session
- 4.7 ppm isoflurane exposure
- NIOSH REL is 2 ppm as a ceiling value.
Sampling Method

- For all sampling events:
  - OSHA method #103
  - low-flow pumps
  - 0.05 liter/minute (LPM)
  - Anasorb 747 Tube
Of Note…

- February 21, 2006 Federal Register requested data and comments on Isoflurane to review the limit
- Isoflurane vs previous anesthetic gases
  - lower blood solubility
  - less biotransformation
  - much decreased hepatotoxicity
  - no effect on fertility, pregnancy, or delivery
  - no evidence of teratogenicity
Old Method

- “Falcon Tube” method
  - closed system
  - Used in ducted biosafety cabinet
- Rest of the process normal
- 6.3 ppm and 2.8 ppm
- Optional XGI-8 Gas Anesthesia System.
- $10,000 extra
Manifold

- Anesthesia manifold
- Confirmed large source of exposure

Anesthesia In

Mouse Noses Go Here
Area Exposure

- Area samples yielded isoflurane concentrations of 3 and 1 ppm.
- Possible exposure to other Animal Resources workers.
Respirators

- Overexposure
- Respirator Program
- Level C PPE
- Uncomfortable
Adding “Optional” Equipment
Vacuum when chamber opened
Charcoal for WAGs
Connections to camera
Flow Control
Almost There

- First sampling with the anesthesia unit gave an exposure of 5.7 ppm.
- There was more tweaking to do:
  - Tubing
  - Pipette Size
  - Oxygen purge
  - Isoflurane flow
Finally

- With all reduction methods in place, 2 more samplings yielded 1.2 and 0.7 ppm.
- Area exposure below detectable limits
- SOP
- Required Training Program
<table>
<thead>
<tr>
<th>Situation/Process</th>
<th>Total # Mice Imaged</th>
<th>Total Sample Time (in minutes)</th>
<th>Isoflurane Concentration (in parts per million)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Older vaporizer</td>
<td>5</td>
<td>20</td>
<td>4.7</td>
</tr>
<tr>
<td>Induction w/ Falcon tube. Maintenance w/ isoflo lines to camera box</td>
<td>10</td>
<td>42</td>
<td>6.3</td>
</tr>
<tr>
<td>Induction w/ Falcon tube. Maintenance w/ isoflo lines to camera box</td>
<td>5</td>
<td>40</td>
<td>2.8</td>
</tr>
<tr>
<td>Inside camera box with 3 mice in manifold and 2 other holes open</td>
<td>3</td>
<td>11</td>
<td>710</td>
</tr>
<tr>
<td>Anesthesia module</td>
<td>14</td>
<td>85</td>
<td>5.7</td>
</tr>
<tr>
<td>All reduction methods in place- dorsal and ventral imaging</td>
<td>7</td>
<td>40</td>
<td>1.2</td>
</tr>
<tr>
<td>All reduction methods in place- intramuscular and intravenous injections</td>
<td>14</td>
<td>80</td>
<td>0.77</td>
</tr>
</tbody>
</table>
Future of Xenogen

- Optional Accessory should be standard
- Increased Use
- High Cost
- Animal Imaging Centers
- Many Researchers with access
- Needs of Animals AND employees in design