Biomedical and Pharmaceutical Manufacturing with Lasers

Ensuring Quality, Compliance and Safety
About the presenter.
Tony Imm

- Founder and CEO of Laser Guardian.
- Certified Laser Safety Officer and Certified Six Sigma Black Belt.
- Member of the ANSI Z136.1 Sub committee for Laser Safety
- Member of the International Electrotechnical Commission (IEC) for Photonic Safety

Laser Guardian is a consulting firm that is focused on Federal and State laser regulatory compliance. This includes validation of laser processes and safety certification of lasers under FDA 21CFR1040.
Subjects covered in this Presentation.
What is a laser and how is laser light generated?

Bio-effects of laser radiation on the eye and skin.

Laser hazard classification and identification.

Compliance to Federal and State Regulations.

Validation Considerations.
SECTION 1
What is a laser and how is laser light generated?
Laser is an acronym which stands for:

- Light
- Amplification
- by the Stimulated
- Emission
- of Radiation
Properties of Laser Light

- **Coherent** – Light waves are in phase.
- **Monochromatic** – A single wavelength is generated.
- **Directional** – Light moves in one direction.
Laser Light, Coherent, Monochromatic and Directional.

How a Laser Works

- Pump on
- Spontaneous emission & rare stimulated emission
- Stimulated emission of light along the laser axis
- Steady state laser operation

○ = atoms in excited state
The first laser had a wavelength of 694 nm

- The first laser light was generated on May 16, 1960.
- The laser itself was invented by Theodore “Ted” Maiman at the Hughes Research Laboratory in California.
- The laser used a ruby rod with silver coated ends that functioned as mirrors. It was excited by a flash lamp that surrounded the ruby rod.
Nd:YAG lasers emit at 1064nm. The active medium is the Nd (neodymium) dopant. The YAG is an Yttrium Aluminum Garnet crystal, which is very optically stable at high temperatures.

Lasers that have their active medium in a crystal rod are also known as solid state lasers.
The optical resonator of the diode laser is between the coated and uncoated facets of the diode and are edge emitting.

The coated (active region) and uncoated (substrate) composition determines the wavelength.

<table>
<thead>
<tr>
<th>Laser diode material (active region / substrate)</th>
<th>Typical emission wavelengths</th>
</tr>
</thead>
<tbody>
<tr>
<td>InGaN / GaN, SiC</td>
<td>380, 405, 450, 470 nm</td>
</tr>
<tr>
<td>AlGaInP / GaAs</td>
<td>635, 650, 670 nm</td>
</tr>
<tr>
<td>AlGaAs / GaAs</td>
<td>720-850 nm</td>
</tr>
<tr>
<td>InGaAs / GaAs</td>
<td>900-1100 nm</td>
</tr>
<tr>
<td>InGaAsP / InP</td>
<td>1000-1650 nm</td>
</tr>
</tbody>
</table>
Construction of a CO$_2$ or HeNe Laser

- The active medium is CO$_2$ or Helium & Neon gas.
- Energy is supplied by a high voltage power supply.
- CO$_2$ lasers are made in the 3-5kW range for laser cutting of steel or 50W range for marking or skin ablation.
- HeNe lasers are usually under 1W and produce a very stable beam. They are used for alignment of optical systems.
Guidelines for selection of a laser.

- Select a laser with a power output in the nominal range of what is needed to process. Laser output tends to vary more at the extremes of the output.
- Select the simplest laser construction for your needs. Complex lasers such as a flash lamp pumped Nd:YAG have more opportunities for output variance.
- Request the FDA accession number from the vendor to better ensure the laser or laser system is compliant.
- Maintain the laser to vendor requirements to keep it operating as designed.
SECTION 2

Bio-effects of laser radiation on the eye and skin.
Beam Hazards

- Hazards found in the laser work environment involving laser energy exposure to eye and skin.

- Hazard types by class:
  - Class 3B Lasers – Eye Hazards
  - Class 4 Lasers – Eye, Skin and Fire Hazards
Retinal Hazards

- Wavelengths 400nm to 1400nm are in the visible and NIR range.
- Beams over 5 mW will damage the eye!
- 5mW = 0.005 watt = 0.005 Joules/second.
  - These are Class 3B and Class 4 Lasers.
  - This is 1,000 times less energy than a 50 watt light bulb.

Laser beams are amplified 100,000 times by the Cornea & Lens and focused on the Fovea where images are processed!
Retinal Hazards

- Examples or eyes with laser damage to the retina.
- Initial effect is rupture of the blood vessels behind the retina followed by loss of site.
- In some cases, some sight may be saved by immediately draining the blood from the affected area.
Ocular Hazards by Wavelength

- **UVB (286-320nm) to UVC (<286nm)** – Photokeratitis, photochemical injury of the corneal epithelium. Symptoms are aversion to light and burning feeling in the eye.
- **UVA (320-400nm)** – Accelerated cataract development.
- **IRB to IRC** – Corneal thermal injury.
If laser exposure is suspected, it is recommended that a Fundus examination of the eye be performed by a knowledgeable ophthalmologist.

Results of the examination should be archived for accident reports and future reference.
Hazards found in the laser work environment other than those involving laser energy exposure to eye and skin.

Typical Hazard Types:
- Electrical Hazards
- Laser Generated Airborne Contaminants (LGAC)
- Compressed Gas.
Electrical Hazards

- Laser have high electrical energy sources such as power outlets, transformers and capacitors.
- The only recorded deaths involving lasers were from electrocution.
Non-Beam Hazard LGAC

- Laser generated airborne contaminates (LGACs).
  - Metals processing.
    - Zinc oxide
    - Cadmium oxide
    - Chromium oxide
    - Nickel oxide
  - Organic and Plastic material processing.
    - Many byproducts are carcinogenic.
    - Benzene, Formaldehyde, Toluene, Styrene, Benzaldehyde.
LGAC Control

- Always use fume extraction.
  - Keeps contaminates off sensitive machine surfaces and optics.
  - Keeps fumes from interfering with the laser beam.
  - Removes contaminates from the work area.
- Use High Efficiency Particulate Air (HEPA) filters to filter out dust and metal fumes.
- Use Charcoal filters to filter our chemical gases and vapors.
Compressed Gas Hazards

• Compressed Gas
  • Secure gas cylinders before and after cylinder change outs.
  • Follow LOTO procedures when handling gas cylinders.
SECTION 3
Laser hazard classification and identification.

DANGER

VISIBLE AND/OR INVISIBLE LASER RADIATION
AVOID EYE OR SKIN EXPOSURE TO DIRECT OR SCATTERED RADIATION

Jones Bldg Rm. 142 – R. Smith

Er:YAG Laser: 2.9 μm, 20 W max, 10 Hz, minimum OD 3.0
Class 4 laser

HeNe Laser: 0.633 μm, 10 mW, minimum OD 1.0
Class 3b laser
All lasers are classified by their hazard potential.

The hazard class of a laser helps one to determine:

- The extent of the laser’s beam hazard.
- The control measures that must be implemented.
- The **Maximum Permissible Exposure** limit.

<table>
<thead>
<tr>
<th>Laser Class</th>
<th>Maximum Permissible Exposure Limit</th>
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<tbody>
<tr>
<td><strong>CLASS 1</strong> and <strong>1M</strong></td>
<td>&lt;.4mW</td>
</tr>
<tr>
<td><strong>CLASS 2</strong> and <strong>2M</strong></td>
<td>≥.4mW to &lt;1mW</td>
</tr>
<tr>
<td><strong>CLASS 3R</strong></td>
<td>≥1mW to &lt;5mW</td>
</tr>
<tr>
<td><strong>CLASS 3B</strong></td>
<td>≥5mW to &lt;.5W</td>
</tr>
<tr>
<td><strong>CLASS 4</strong></td>
<td>≥.5 Watt</td>
</tr>
</tbody>
</table>
Warning Label

This label is used to identify the exit location of the laser beam. It is referred to as an aperture label. This label is required by 21CFR1040.10.

![Avoid Exposure Label](Image)

Label is bold black type on a yellow background. It is located near the exit location of the laser beam. Typically located on the focal head.
Warning Label

This label is used to identify laser hazard level. This label is required by 21 CFR 1040.10 for a class 4 laser.

Position 1 states “LASER RADIATION. AVOID EYE OR SKIN EXPOSURE TO DIRECT OR SCATTERED RADIATION”

Position 2 contains type of laser or wavelength, pulse duration and maximum output.

Position 3 states “CLASS IV LASER PRODUCT”
Control Measures

- **Engineering**
  - Equipment specific
  - Meet ANZI Z136.1 and Florida code 64E-4
  - **Examples:**
    - Protective Housing
    - Interlocks
    - Warning Labels
    - Temporary Controlled Area

- **Administrative**
  - Describe safe practices
  - Meet ANSI Z136.1 and Florida code 64E-4
  - **Examples:**
    - SOPs
    - Training
    - Authorized Staff
    - PPE
Guidelines for laser safety.

- Laser safety programs need to be fully supported by management.
- Develop a laser safety program prior to putting a laser into production. This includes identifying a LSO (Laser Safety Officer).
- Train all employees in laser safety awareness. The reduces the “fear of the unknown”.
SECTION 4
State and Federal Regulations.
Florida Laser Regulation

- The state of Florida uses administrative code 64E-4 to control laser radiation hazards.
- It is administered by the Florida Department of Health.
- The code is based on and follows many of the requirements of ANSI Z136.1 American National Standard for Safe Use of Lasers.
- 64E-4 has additional requirements over ANSI Z136.1.
  - All lasers that are hazard class 3B or 4 must be registered with the state. This includes lower class lasers that maybe hazard class 3B or 4 during servicing.
  - Regular laser audits, at least semi-annual, must be performed and documented.
  - Laser accidents must be reported to Florida DOH. Compliance time is based on the seriousness of the accident. 3rd degree burns, death or exceeding 100 times the MPE must be reported within 24 hours.
ANSI Z136.1-2014 is 255 pages in length and contains many examples and illustrations on how to comply. Training is available through the Laser Institute of America or other sources.

Compliance with ANSI Z136.1 is voluntary.

64E-4 is 13 pages in length and contains only a definition section of terms used. Florida DOH does not offer compliance training. Training is available through Laser Guardian LLC.

Compliance with 64E-4 is mandated by the State of Florida.
Center for Devices and Radiological Health (CDRH) regulates the safety of lasers and laser systems sold within the United States.

Lasers or laser systems that are sold to the public must be compliant with a number of federal regulations to include FDA 21CFR1040.

Lasers and laser system certification documents are submitted to the CDRH using FDA form 3632.

“WE DO NOT APPROVE THESE REPORTS OR THE PRODUCTS BEING REPORTED. It is the manufacturer’s responsibility to certify that their products comply with all applicable standards (21 CFR 1010 - 1050), based on a testing program in accordance with good manufacturing practices.” FDA form 3632 Forward.
OSHA Requirements

- OSHA has no specific laser safety requirements except for the construction industry.
- “Each employer shall furnish to each of his employees employment and a place of employment which are free from recognized hazards that are causing or are likely to cause death.” General Duty clause from the OSH act of 1970.
- ANSI Z136 is a recognized standard to be used for compliance to the “General Duty” clause.
SECTION 5
Validation
Run a DOE (design of experiment) for most laser processes to understand the interaction of the inputs to get the desired response.

Focus on Method, Material and Machine.
Use the correct pulse width, pulse rate and pulse profile.
- Pulse width is how long a beam needs to be energized on target to get the proper response.
- Pulse rate is used to apply short bursts of energy on target. A spot welding process may require multiple pulses on the same area to deliver sufficient thermal energy without evaporating the target material.
- Pulse profile is the temporal shape of each pulse. This may be needed to apply a low initial energy to heat soak a material then apply higher energy for welding.

When ablating material from a substrate it may be necessary to make multiple overlapped passes to remove the material without overheating the substrate.

Beam reflection due to the curved shape of the process material must be considered when developing a process.
Use the correct wavelength for your process.

- photo-thermal than use a wavelength that will deliver heat to the process area. Typically this is near infra red (NIR).
- If the process is photo-chemical, use a wavelength that will break the molecular bonds with minimal photothermal effect. Typically this is in the UV range and involves plastics.

Recommend that a spectral analysis be performed to determine what wavelengths are absorbed by the material.

- NIR a great wavelength for welding stainless steel. However, copper will reflect much of these wavelengths.

Understand the necessary beam profile which has spatial and temporal characteristics.

- Spatial – Top hat or Gaussian
- Temporal – The rise and drop of the beam energy during the pulse.
Micro contamination by foreign materials or oxides of the component metal can affect process performance. This is especially true for soldering processes.

When welding dissimilar metals, they must have an overlap between their melting point and boiling point.

Material quality may vary from vendor to vendor and batch to batch. Ensure that the vendor has a controlled process and the processed material performs consistently within your process limits.

Surface finish can affect the lasing process by varying the reflectivity of the beam.

- Run acceptance tests based on your Equipment Specification document prior to accepting equipment.
- Run a DOE to understand input interactions.
- Lasers will degrade over time. Characterize and document the laser output before it is introduced into production.
- Validate the actual process inputs.
  - Validate the energy required to perform the process not the laser set point needed to generate that energy. i.e. a laser generates 10 joules at 45% of diode current.
- Monitor the laser output on a regular basis to alert of degradation before it affects the process.
The use of process lasers in the medical device and pharmaceutical industries, as with all manufacturing, will continue to grow.

Lasers are not a simple light/energy source. Thorough due diligence is required before selecting a laser process.

Always document and train, do not rely on “tribal knowledge”.

Implement and sustain effective laser maintenance and safety programs. Verify by conducting regular audits.

Because the key to laser Quality, Compliance and Safety is knowledge.