



# SOAPS

**October 26-30, 2003  
Salt Lake City, Utah**

H  
I  
N

H

H  
Hydrogen

Lithium 6.941  
Beryllium 9.0122

Na 22.9898  
Mg 24.312  
Sodium Magnesium

19  
K 39.102  
Potassium

20  
Ca 40.08  
Calcium

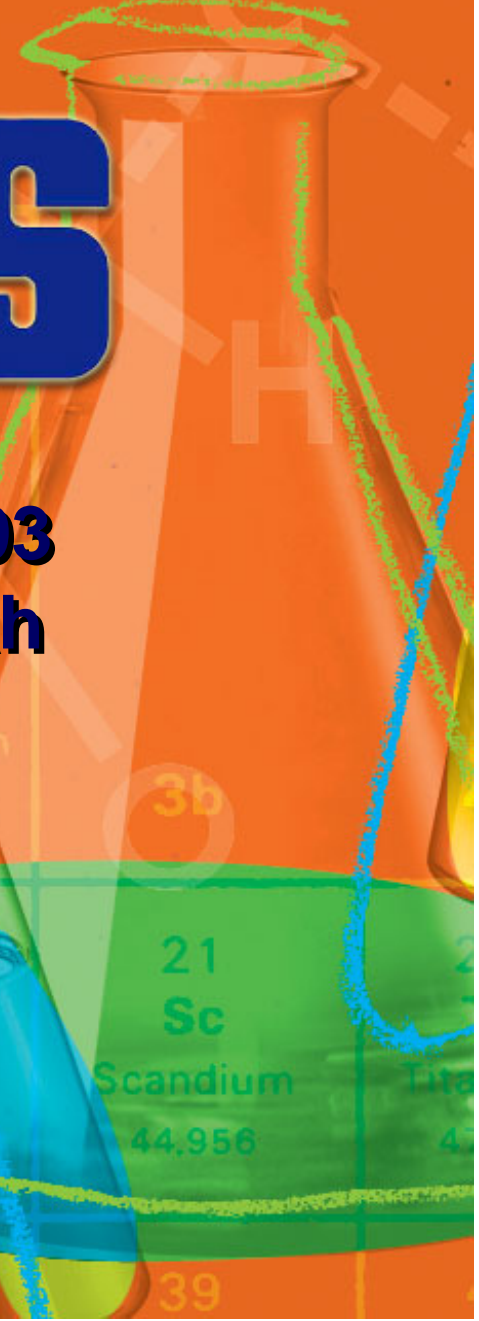
21  
Sc 44.956  
Scandium

3b

37

38

39



# High Energy Pulsed UV Light as a Sterilization Process

American Association of Pharmaceutical Scientists –  
Annual Meeting and Exposition

**October 27, 2003**

**Presented by**

**Louis Panico, CEO**

# UV Sources

- Basic techniques to generate UV light
  - Continuous
  - Pulsed
- Sources of plasma-generated UV radiation
  - Electric arc
  - Mercury lamp
  - Pulsed xenon flashlamp

# Conventional UV vs. Pulsed UV

## Conventional UV

- Mercury lamp
- Monochromatic light - 254nm
- Long exposure times
- Generates heat
- Repair of DNA dimers
- Not capable of sterilization
- Loss of energy from lamp during continuous emission

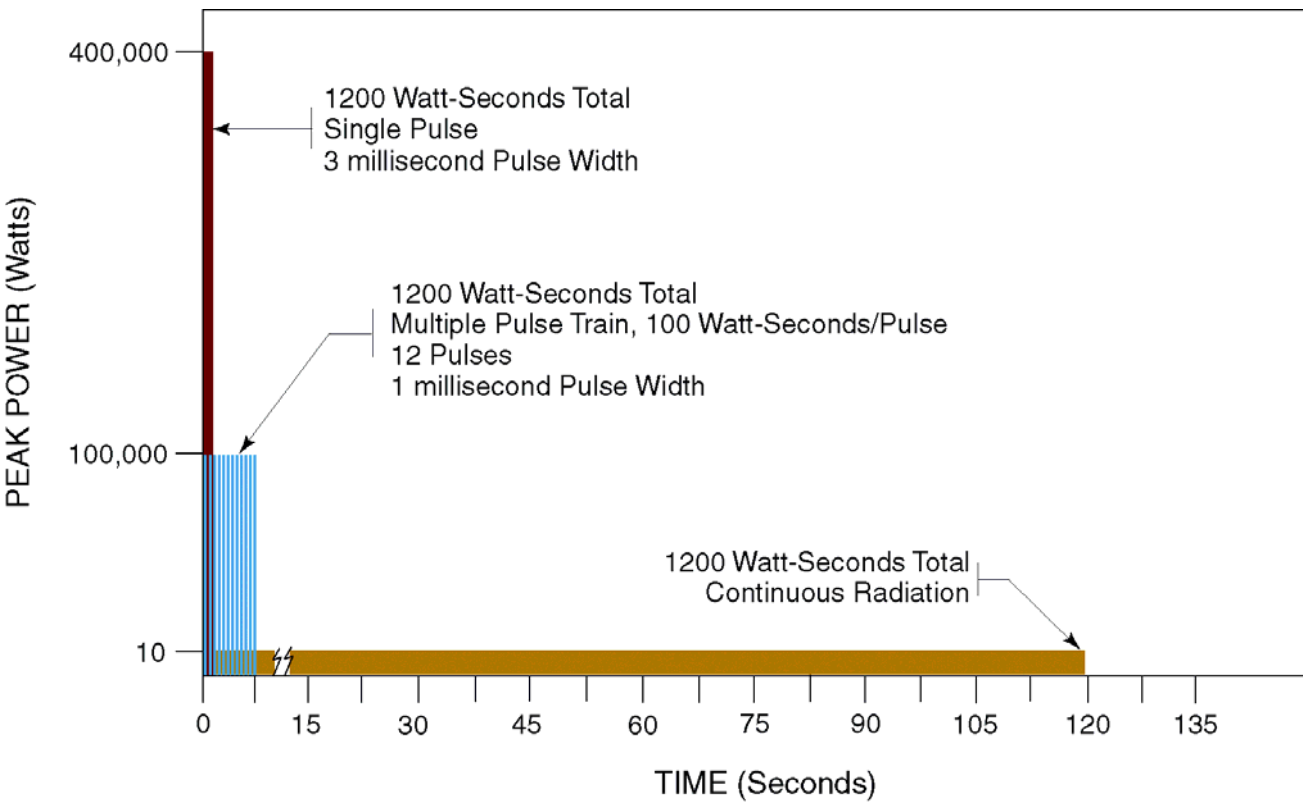
## Pulsed UV

- Xenon inert gas
- Broad spectrum - 200-1100 nm
- Very short exposure time (seconds – minutes)
- No significant heat generated
- DNA strand breakage--No evidence of repair mechanism
- Achieves USP sterility levels
- No loss of lamp energy between pulses

# Why Pulsed UV Light?

- Generates wideband radiation – 50 nm to 5 microns
  - Especially rich in UV spectral region 180 nm to 400 nm
- Highly efficient for UV light generation
  - 50% to 60% of input electrical energy converted to optical energy
- Environmentally benign
  - Does not use toxic materials such as mercury
  - Does not create suspended airborne particulates
- Pulsed UV systems provide unique attributes
  - Very high peak power .. As high as  $1 \times 10^6$  watts
  - Low surface temperature buildup
  - Instant on/off control
  - Multishaped lamps match application requirements

# Comparison of Pulsed UV and Continuous UV



Pulsed light is illustrated in a single pulse and burst mode

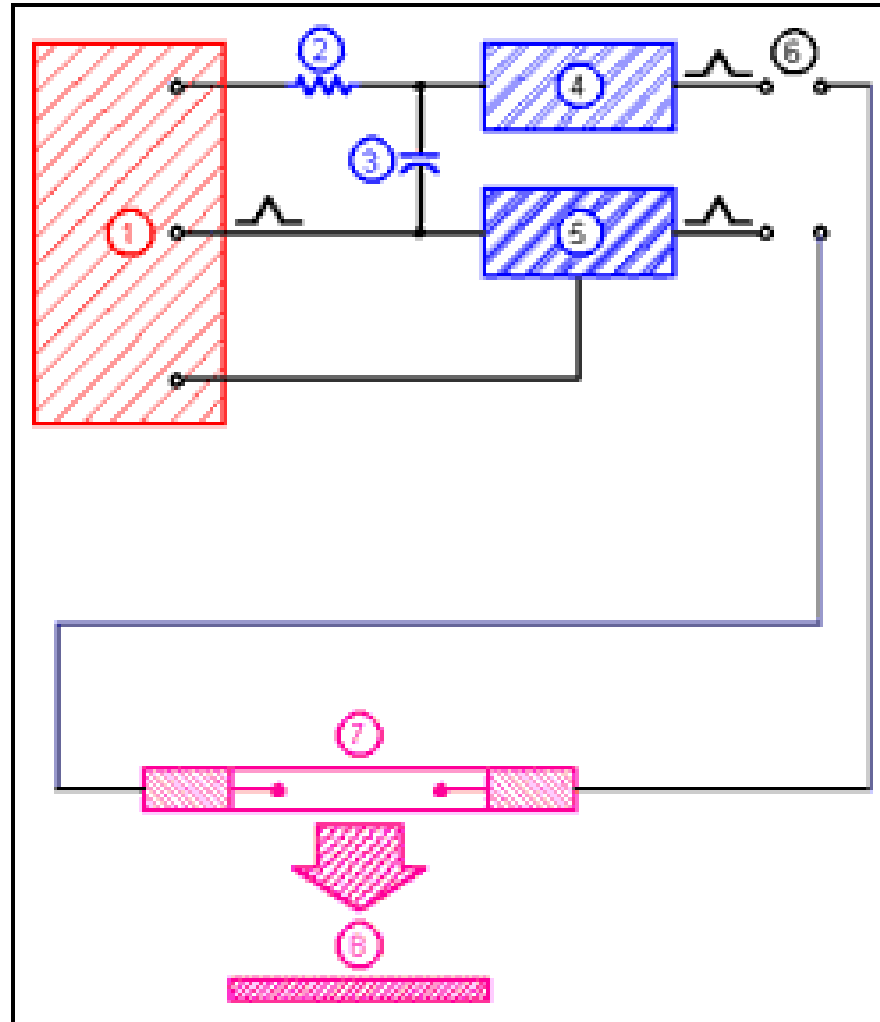
# Pulsed UV

## System components

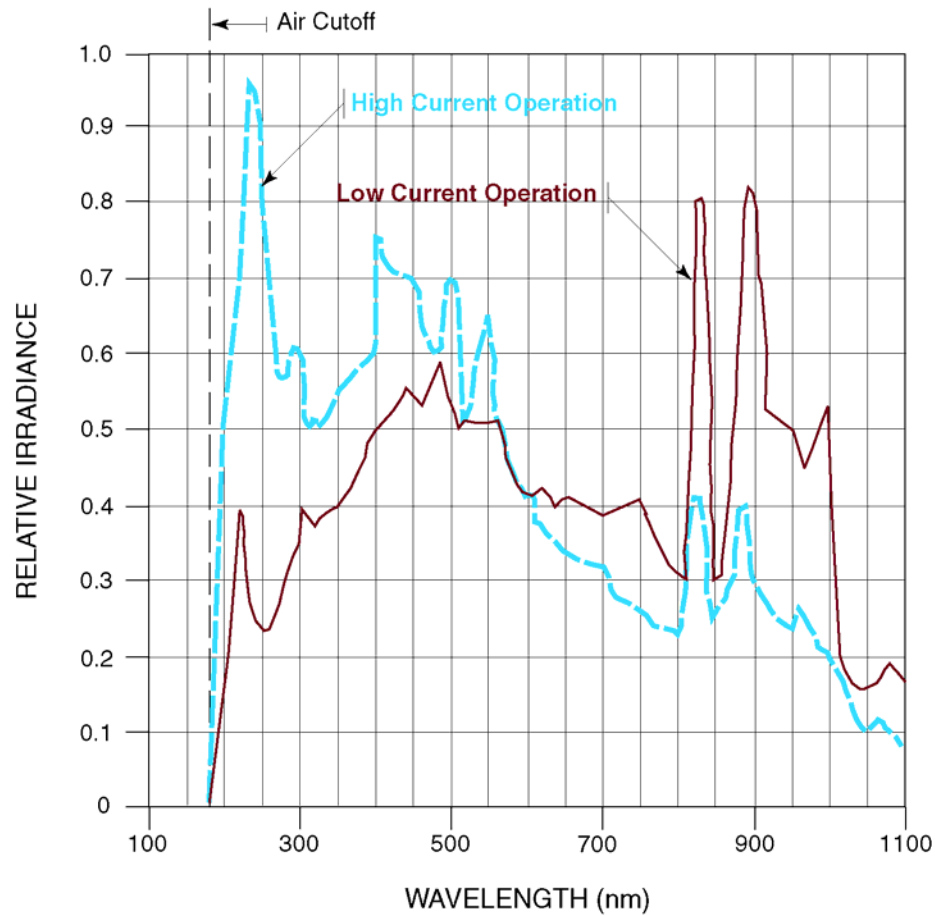
- High voltage power supply
- Pulse forming network (PFN)
- Flashhead module
  - Incorporates UV optics
- Blower or cooling system for flashhead module
  - Effectiveness will determine operation and life of the UV source
- Control Module

# Block Diagram

## - Pulsed UV Light System

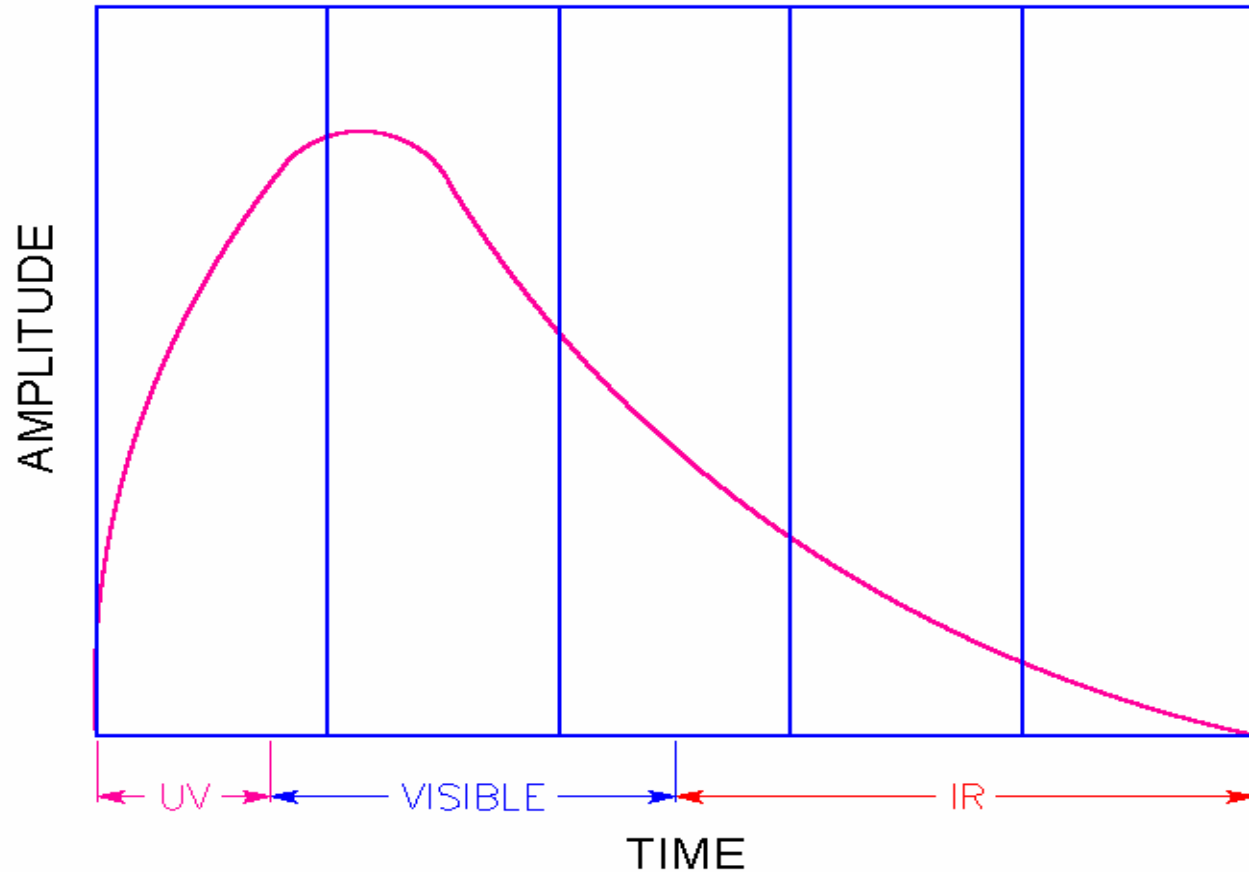


# Spectral Dependence on flashlamp operating parameters



# Spectral Components

- a single pulse of light



# Pulsed UV Exposure

## - effects on microorganisms

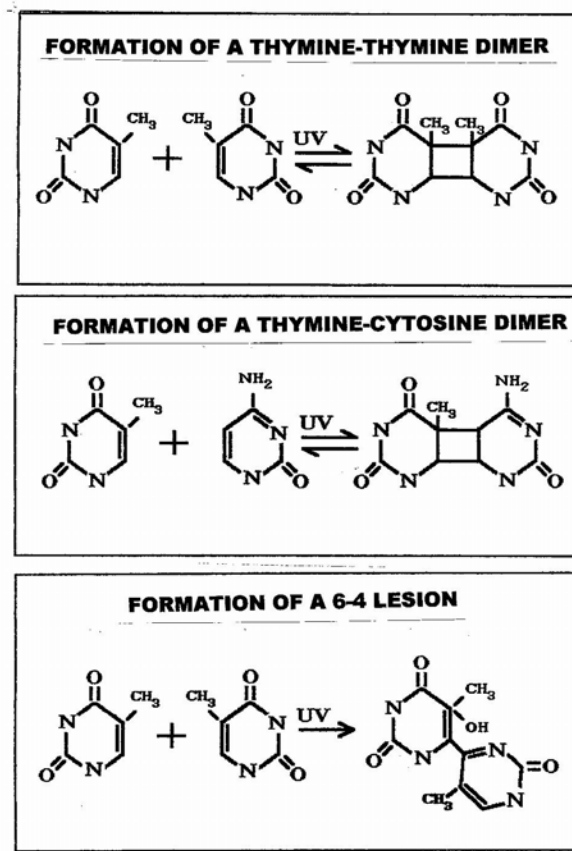
- Provides effective means of photophysical and photochemical reactions of light absorption by molecules
- Produces chemical pathways such as short-lived chemical species, charge-transfer reactions and energy transfer phenomena in chemical biological systems
- Primary process in sterilization of microorganisms is by destroying DNA and RNA

# Mechanisms of Action of Pulsed UV

- DNA: Demonstration of strand breaks and dimer formation in vivo and vitro
- RNA: Single stranded breaks and formation of dimers
- Proteins: Peptide bonds not broken; Inactivation of enzyme activity controlled or minimized by controlling the delivery of critical parameters
- Membrane Effects: Under investigation using platelets and bacteria as model systems.

# UV Exposure

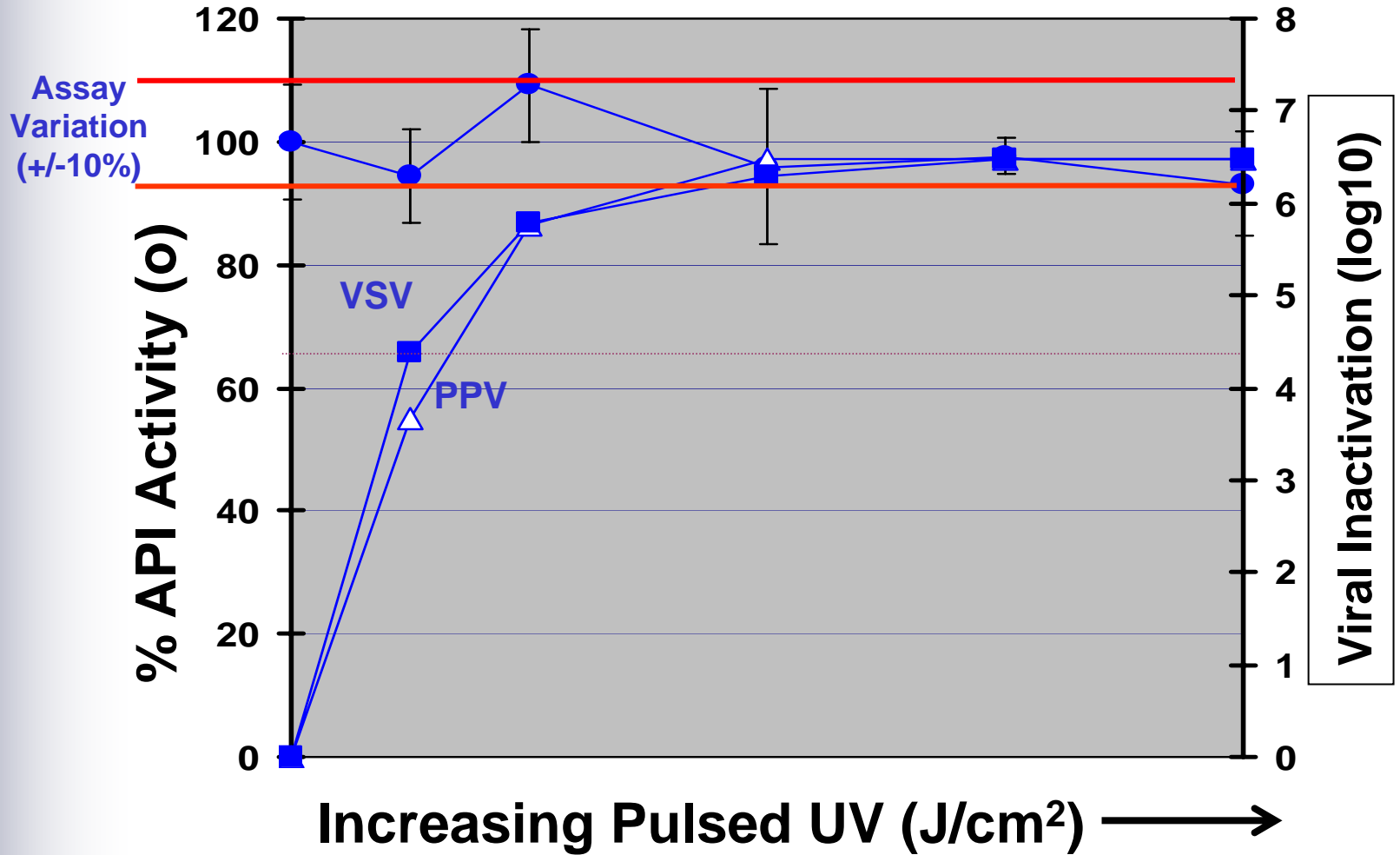
## - Formation of Dimers and 6-4 Lesions



- DNA damage caused by UV exposure includes formation of pyrimidine dimers and (6-4) photoproducts
- These damages result in mutations, impairment of replication and gene transcription – leading to the death of the organism
- Cells have evolved mechanisms for repairing DNA damage
- Pulsed UV radiation leads to ultimate genetic destruction of microorganisms
  - Ability to adjust light intensity
  - Ability to adjust pulse duration
  - Ability to select number of pulses

# >6 Log Non-Enveloped Virus Reduction

Showing Complete Recovery of API After Exposure to Pulsed UV



# Opportunities with Pulsed UV

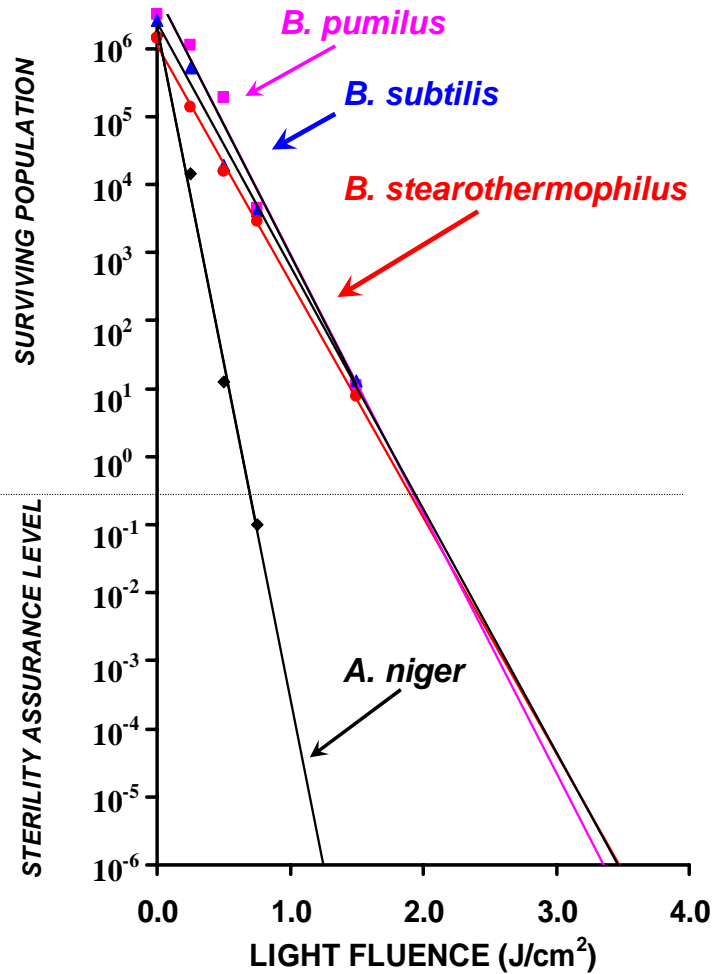
- Virus Inactivation of enveloped and non-enveloped viruses
- Decontamination of high purity water systems
- Terminal sterilization of Blow/Fill/Seal containers
- Terminal Sterilization of medical devices and packaging arrangements

# Surface Sanitization

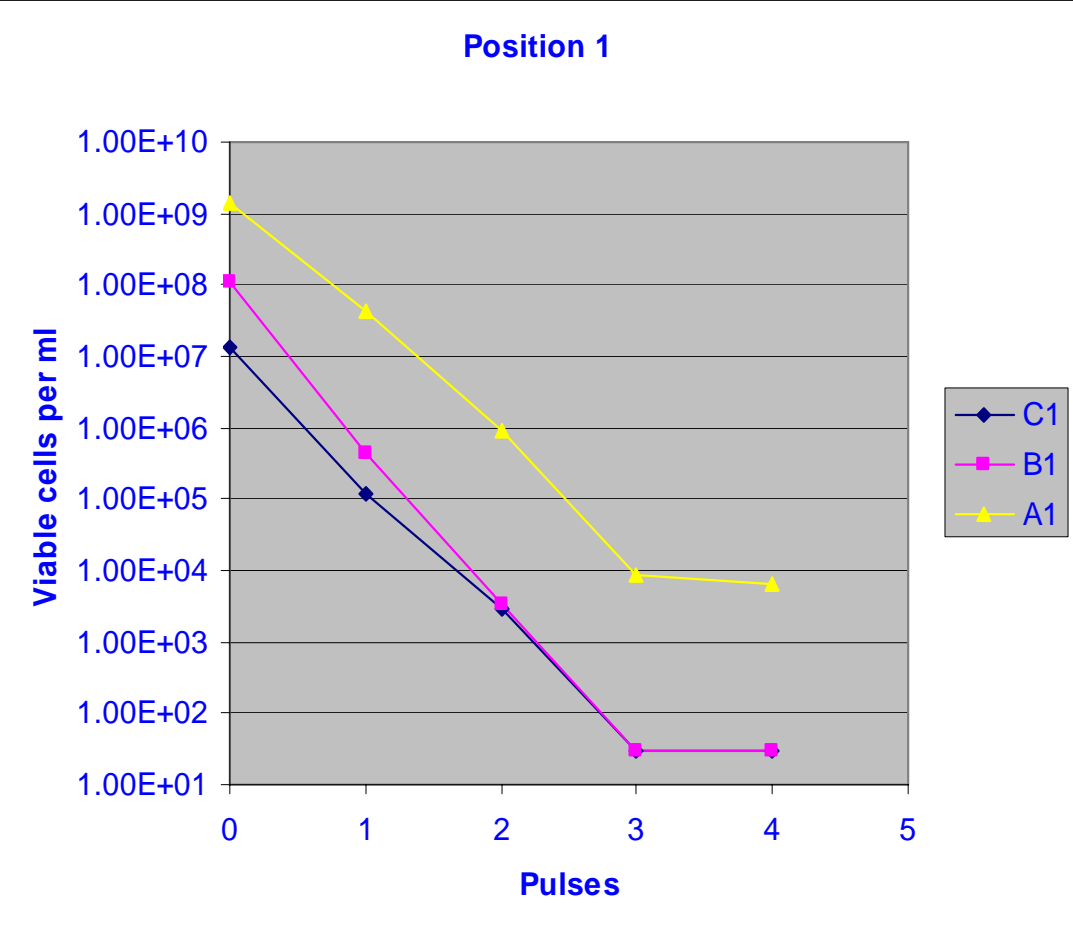
- results from tests on bacteria spores

- Pulsed UV light has been shown to be effective in applications requiring surface sanitization
- Tests performed on spores using Pulsed UV
  - Type produced by Bacillus and Clostridium species
  - Known to be resistant to various forms of radiation and other physical & chemical agents
  - Spore samples irradiated with pulsed UV light

# Dry Surface Survival Kinetics



# Viability of *bacillus subtilis* spore samples exposed to UV pulses



Samples located on the flashlamp axis and at the mid point of the flashlamp

Figure provided by Abraham L. Sonenshein, PhD  
Department of Molecular Biology and Microbiology  
Tufts University School of Medicine

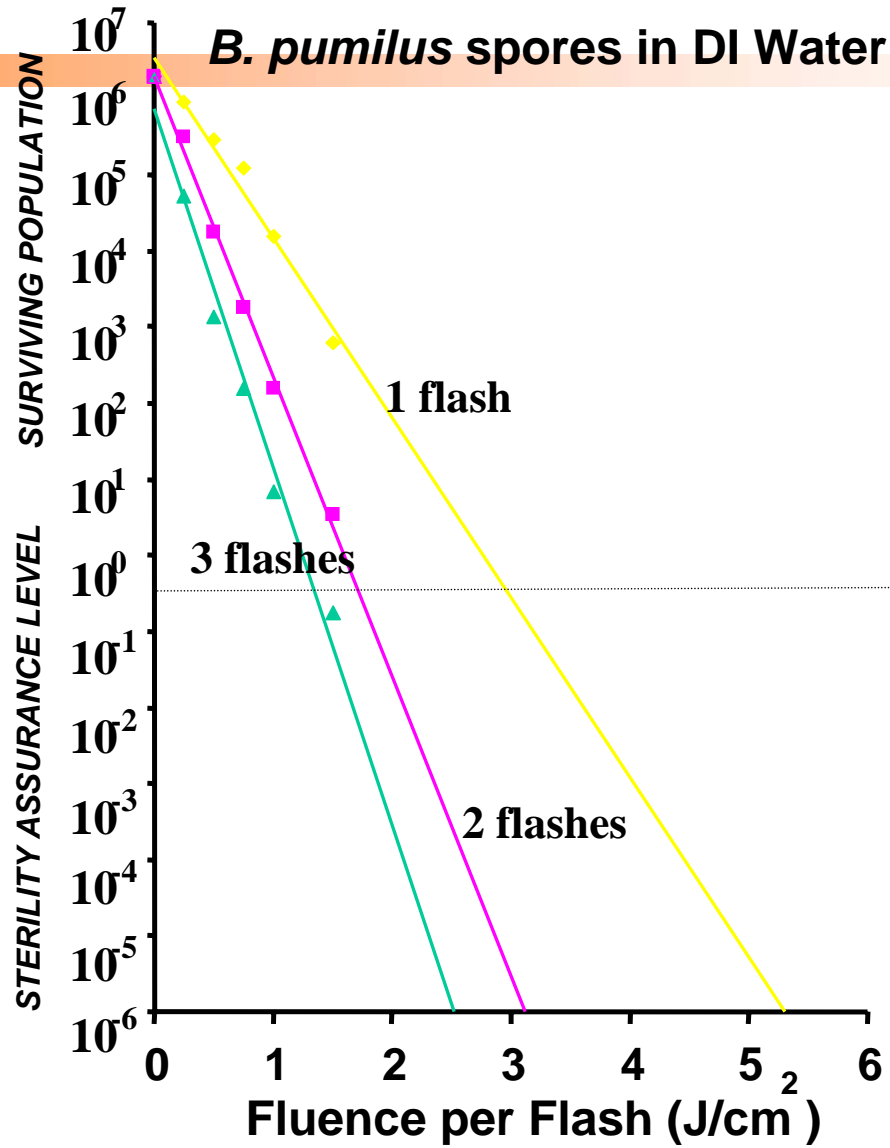


# Sterilization of Static Liquids in 20 ml BFS Vials

Organism	Inoculation (in 20 mL)	Sterility Test Result <sup>1</sup>		
		Glucose	Saline	WFI
<i>Bacillus subtilis</i> var. niger spores	4.8 x 10	Pass	Pass	Pass
<i>Bacillus pumilus</i> spores	3.0 x 10	Pass	Pass	Pass
<i>Bacillus stearothermophilus</i> spores	4.4 x 10	Pass	Pass	Pass
<i>Clostridium sporogenes</i> spores	2.4 x 10	Pass	Pass	Pass
<i>Aspergillus niger</i> spores	1.4 x 10	Pass	Pass	Pass
<i>Candida albicans</i>	3.0 x 10	Pass	Pass	Pass
<i>Deinococcus radiodurans</i>	2.2 x 10	Pass	Pass	Pass
<i>Staphylococcus aureus</i>	5.6 x 10	Pass	Pass	Pass
<i>Enterococcus faecalis</i>	2.0 x 10	Pass	Pass	Pass
<i>Escherichia coli</i>	3.4 x 10	Pass	Pass	Pass
<i>Salmonella choleraesuis</i>	1.8 x 10	Pass	Pass	Pass
<i>Pseudomonas aeruginosa</i>	2.8 x 10	Pass	Pass	Pass

<sup>1</sup> Treatment level was approximately 4.5 J/cm<sup>2</sup> per flash, with 2 flashes. 20 replications for each liquid/microbe combination. No dark or light enzymatic repair of nucleic acids after 28 days of incubation.

# Static Liquid Survival Kinetics



# Model Viruses Tested with Pulsed UV

**SV40**

**Canine Parvovirus**

**Porcine Parvovirus**

**Simian Rotavirus (SA11)**

**Bacteriophage PRD-1**

**Poliovirus Type I**

**Reovirus**

**Bacteriophage MS-2**

**Encephalomyocarditis Virus (EMC)**

**Hepatitis A Virus**

**Human Immunodeficiency Virus (HIV-1)**

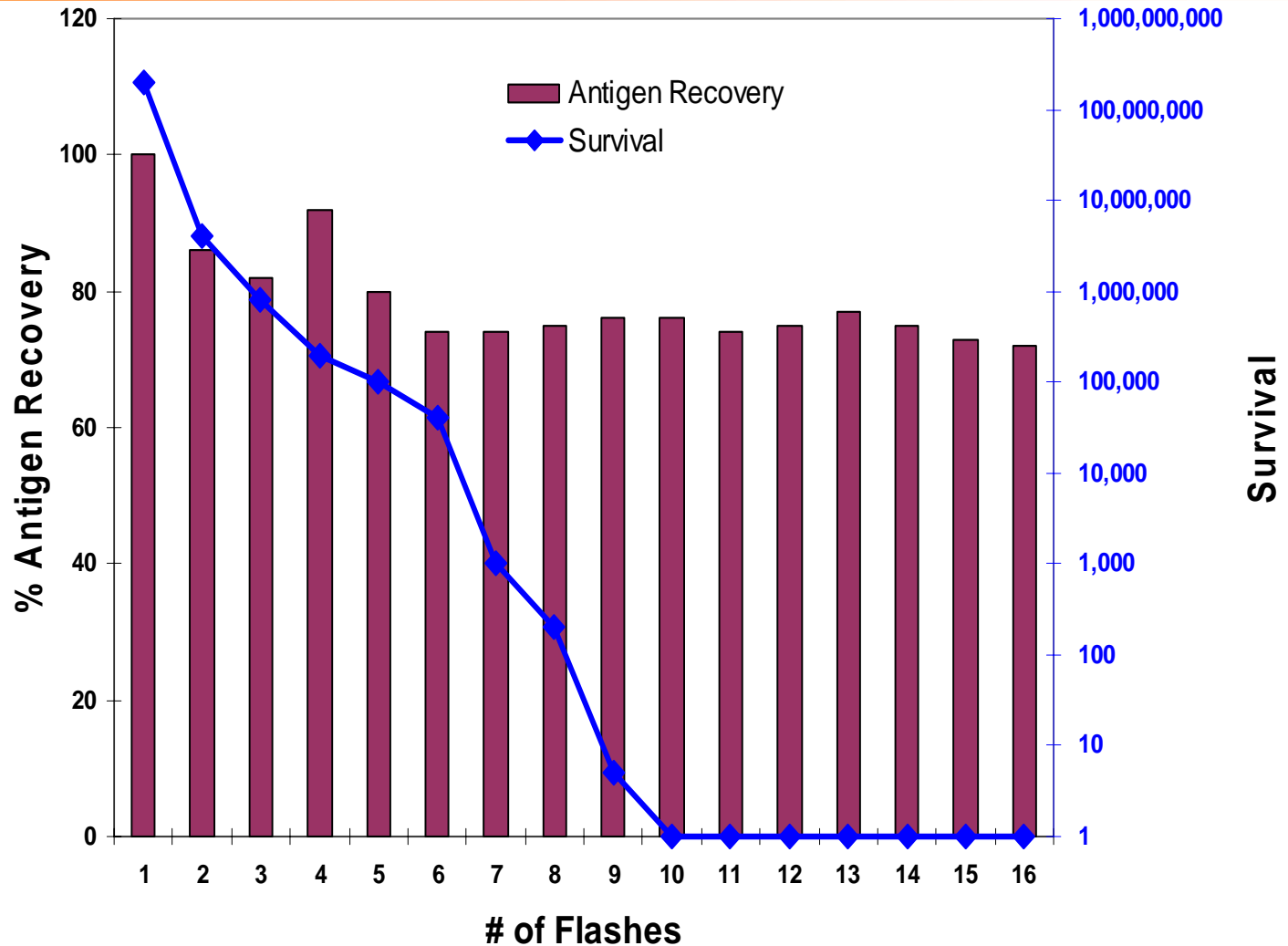
**Bovine Viral Diarrhea Virus (BVDV)**

**Sindbus Virus**

**Vaccinia Virus**

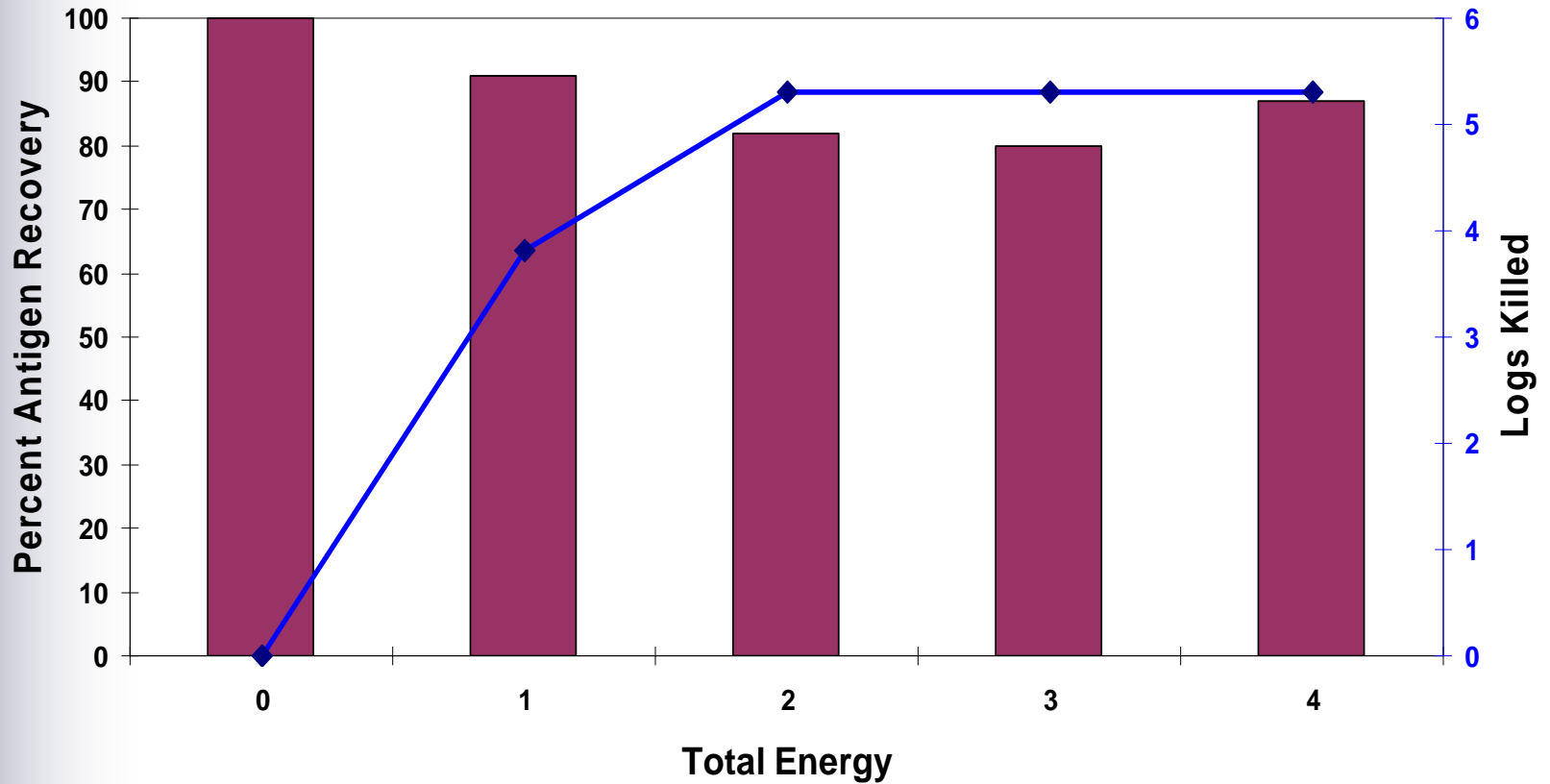
**Vesicular Stomatitis Virus**

# Pulsed UV Demonstrates Complete Inactivation of a Cancer Causing Virus with High Antigen Recovery



# Complete Inactivation of Herpes Simplex Virus I with High Antigen Recovery

Reproduced courtesy of Dr. David Katz, Univ. of Georgia State



# Validatable with Real Time In-Process Monitoring

- **UV and full spectrum (FS) monitors**
  - **FS fluence (lamp and product)**
  - **UV fluence (lamp and product)**
  - **Transmission**
  
- **Error checking**
  - **Product flow rate**
  - **Lamp current**
  - **Load cell force**
  - **Flash rate**
  
- **Product temperature**

# Regulatory Status of Pulsed UV

- **In-line sterilization of thin films for producing IV bags**
  - **Cleared by FDA for production**
- **Terminal sterilization of interstitial space of packaging arrangement**
  - **In production in Canada**
- **Terminal sterilization of blow/fill/seal parental diluents**
  - **In production in Japan for over 3 years**
- **Terminal sterilization of microchip implant device**
  - **Phase III clinical trial in USA**
- **Barrier isolator device undergoing validation in Europe**
- **Laboratory scale in-flow virus inactivation device undergoing validation in treating plasma derivative products**

# Application of Pulsed UV

## -implantable medical device production



- Ease of integration into automated manufacturing environment
- Example shown : complete curing of a lubricious coating on medical guide wires

*Photo courtesy Guidant Corporation*

# Terminal Sterilization - Syringe



# Pulsed UV Summary

- **EFFECTIVE  
INACTIVATION**
  - **Achieve USP 10<sup>-6</sup> SAL**
  - **No microorganism found resistant to Pulsed UV**
  - **No repair of nucleic acids**
- **SELECTIVE  
BIOMOLECULAR  
DESTRUCTION**
  - **Destruction of DNA/RNA**
  - **High antigen recovery**
  - **No significant heat effect on product**
- **RAPID &  
CONTROLLED  
PROCESS**
  - **Single step process**
  - **Treatment in minutes (per liter)**
  - **Broad spectrum fluence monitoring**
- **SAFE**
  - **No toxic chemicals or ionizing irradiation**
- **SCALABLE**
  - **200 ml/min to >10 L/min.**