Wildfire Smoke: Focus on Non-viable Particles and Sterile Compounding for Pediatric Patients

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Fire between Lynn and Salem, 20 miles north of Boston

~130 acres at its peak

Triggered a HICS response due to the overwhelming smell of smoke inside the hospital – complaints from patients and staff

Public Affairs had to create messaging that the hospital was not on fire nor in danger, concern for resp exacerb

Engineering routed fresh air intake to mix with recirculated HEPA filtered air where possible

Smoke hanging over Boston as North Shore wildfire blazes

Smoke cloud hanging over the Boston area is coming largely from a major brush fire to the north between Lynn and Salem. (Photo By Naomi Zottoli/Boston Herald)

Pediatric health, air pollution and wildfire smoke

- Respiratory disease
  - Increased exposure to air pollutants increases risk of respiratory infections in the first year of life (Amodio)
  - Increased rates (over 200% in some cases) in visits for asthma exacerbations, even if significant distance from the fire (example NYC ED visits during Canadian wildfires)
  - Wildfire smoke $PM_{2.5}$ is approximately 10x more harmful to pediatric resp health than $PM_{2.5}$ from other sources (Oerther, Aguilera)
  - Disproportionally affects socioeconomic disadvantaged communities

Pediatric health, air pollution and wildfire smoke

- Other disease states
  - Shapiro et al found that patients were less likely to seek care in EDs for headache treatment on days with high smoke burden, different from adult literature where headache visits increase
    - Turned into a health care utilization study
  - Oerther and colleagues reviewed 16 studies related to pediatric health in wildfires. Increased rates of anxiety, depression, PTSD, suicidal ideation – some link to smell of smoke, not just threat of a disaster
    - Physical health – corneal abrasions, eye irritation
    - Children do not appear to have the same cardiovascular exacerbation risk as adults


DOSEEDGE

Cleanroom particles

- Deemed by ISO 14644-1:2015 Standard

- ISO Classifications for air quality are determined by how many particles (viable and non-viable) > 0.5 microns are in the space *under dynamic conditions*
  - ISO 5 = “hoods” = < 3520 m^3
  - ISO 7 = buffer room, anteroom *if* connected to negative pressure buffer room = < 352,000 m^3
  - ISO 8 = anteroom = < 3,520,000 m^3
  - ISO 7 spaces must have a minimum of 30+ Air Changes Per Hour (ACPH)

- Measured with light scattering airborne particle counter every 6 months per USP 797

ISO = International Organization for Standardization

USP = United States Pharmacopeia

Pharmacy Sterile Compounding Cleanroom Operations

Images: https://www.aaoallergy.org/usp-general-chapter-pharmaceutical-compounding-sterile-preparations/

- More controlled than any OR setting
- Strict garbing and hand hygiene requirements
- Strict cleaning requirements, for the room, hoods and all supplies
- Strict equipment operation protocols
- SOPs are written and trained against
  - Augmented Reality assisted training
  - Competency assessed q6months with microbial testing of glove fingertips and surface sampling as well as media fill
- Periodic oversight in the cleanroom by a pharmacist or lead tech
- Discussion of the “why” at every staff meeting
- Adherence is driven by the individual
  - Slips, Mistakes, Workarounds
  - Ergonomics
  - Environment

Non-viable particles

- What increases the particle load in a space?
  - PEOPLE! Normal skin sheds 40,000 cells per hour – this equals 3.6 kg/8 lbs in one year!
  - Pharmaceutical ingredients and adjuvants (e.g preservatives, oxidizers, etc), containers, gloves
  - Paper (forms, labels, boxes, syringe wrapper backing, glove packaging, wipes, etc)
  - **Air pollutants**

- Monitoring
  - A snapshot in time, current processes are too intrusive to workflow to be conducted continuously and may actually generate more particles
  - Limitations include operator variability, testing location variability, equipment maintenance, lower levels of detection


LIFESTRAW PURIFICATION
0.02 µm
Removes viruses and ultra-small particles.
LIFESTRAW FILTRATION
0.2 µm
Filters bacteria and parasites.
VIRUS
0.02–0.3 µm
Such as norovirus or hepatitis A.
BACTERIUM
0.5–5 µm
Such as E. coli or Salmonella.
RED BLOOD CELL
7–8 µm
Carries oxygen throughout your body.
FINE AIR PARTICLES (PM2.5)
2.5 µm
Fine inhalable dust from smoke, pollution, and other sources.
POLLEN GRAIN
10–20 µm
Can trigger allergies and hay fever.
WHITE BLOOD CELL
20 µm
Helps your body fight infection.
GRAIN OF SALT
60 µm
FINE BEACH SAND
90 µm
HUMAN HAIR
50–180 µm
For scale.
LifeStraw.com

PROCEDURE:
OPERATIONAL Particle counts were taken as specified in ISO 14644-1 with sample durations of 1.0 minute on size discrimination of 5.0 microns.

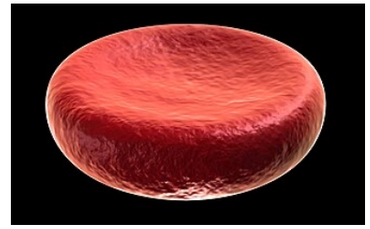
Probe was positioned approximately 40" above floor facing vertically upward.

DESIGN REQUIREMENTS:

ISO Class 5	≤ 29 particles/cubic meter ≥ 5.0 microns
ISO Class 7	≤ 2,930 particles/cubic meter ≥ 5.0 microns
ISO Class 8	≤ 29,300 particles/cubic meter ≥ 5.0 microns

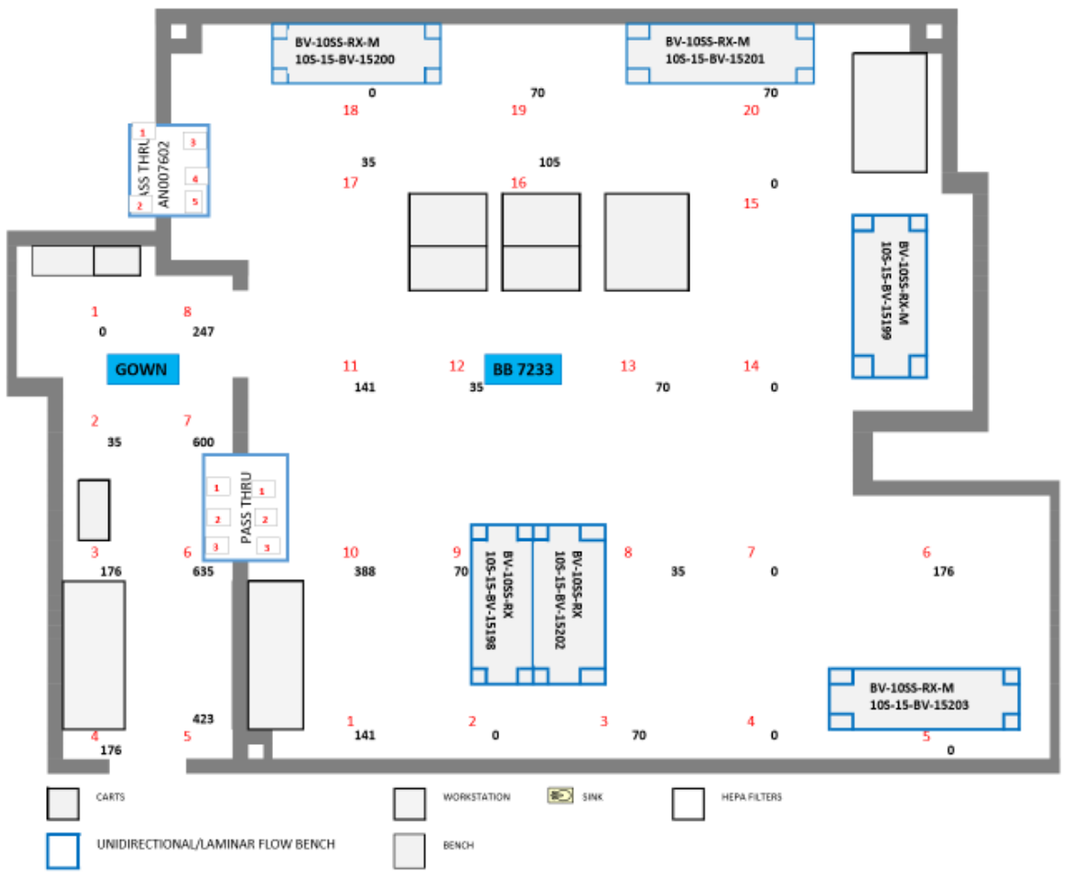
RESULTS:
The results are as follows:

Area	MAXIMUM (particles/m^3)	ISO CLASS LIMIT (particles/m^3)	DESIGNATED ISO 14644-1 Classification ≥ 5.0 microns	RESULT
IV PREP 7233	388	2,930	7	PASS
ANTE ROOM	635	29,300	8	PASS
PASS THRU AN007602	0	29	5	PASS
IV - ANTE PASSTHROUGH	105	2,930	7	PASS
ANTE - IV PASSTHROUGH	105	2,930	7	PASS



A human Red Blood Cell is 5 microns

PARTICLES/M^3 ≥ 5.0 µm



* PLEASE NOTE - NOT TO SCALE!

PROCEDURE:

OPERATIONAL Particle counts were taken as specified in ISO 14644-1 with sample durations of 1.0 minute on size discrimination of 0.5 microns.

Probe was positioned approximately 40" above floor facing vertically upward.

DESIGN REQUIREMENTS:

ISO Class 5	≤ 3,520 particles/cubic meter ≥ 0.5 microns
ISO Class 7	≤ 352,000 particles/cubic meter ≥ 0.5 microns
ISO Class 8	≤ 3,520,000 particles/cubic meter ≥ 0.5 microns

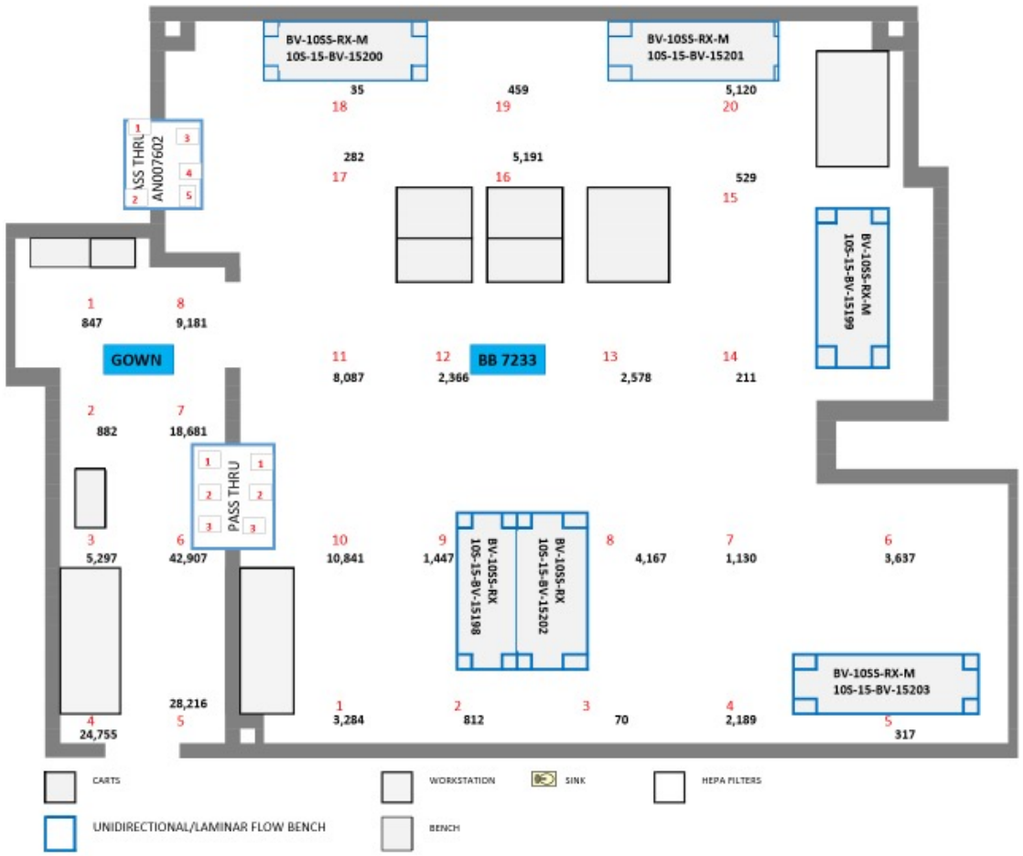
RESULTS:

The results are as follows:

Area	MAXIMUM (particles/m^3)	ISO CLASS LIMIT (particles/m^3)	DESIGNATED ISO 14644-1 Classification ≥ 0.5 microns	RESULT
IV PREP 7233	10,841	352,000	7	PASS
ANTE ROOM	42,907	3,520,000	8	PASS
PASS THRU AN007602	0	3,520	5	PASS
IV - ANTE PASSTHROUGH	18,081	352,000	7	PASS
ANTE - IV PASSTHROUGH	7,592	352,000	7	PASS

Smoke particles are ~ 0.5 microns (image NYT)

PARTICLES/M^3 ≥ 0.5 µm



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Why does it matter?

- Majority of literature focuses on inhalation of Particulate Matter (PM) and effects on respiratory health
- Unknown effects when ingested, absorbed or injected
- USP 788 – Particulate Matter in Injections
  - Mobile, unintended particles
  - Spherical particles between 10-25 microns (micrometers) are identified by light obscuration and light microscopy, both methods have limitations and are not routinely performed outside of pharmaceutical manufacturing facilities
  - Pyrogens

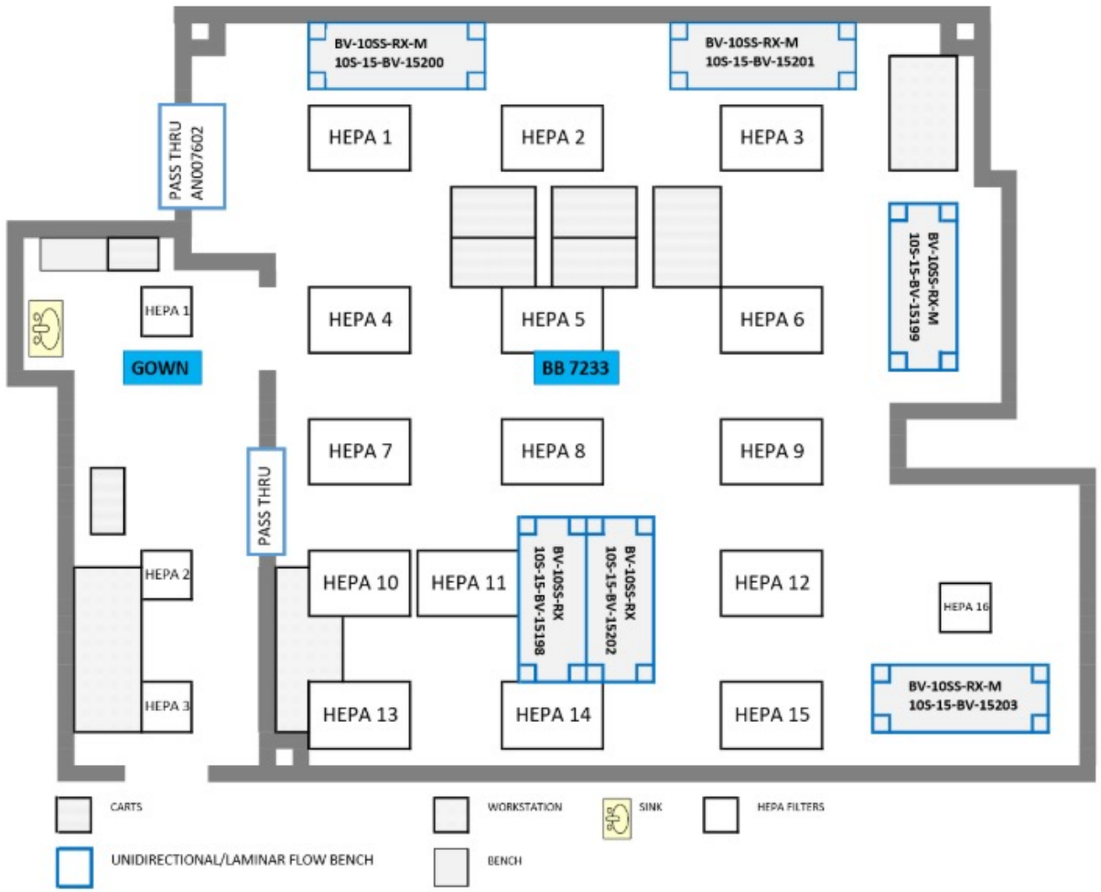
What do we do to clean the air?

- HEPA filters
  - AHU, ceiling and in the vertical flow hoods
  - Integrity is tested every 6 months
  - Removes > 99% of particles > 0.3 microns

- Air source
  - Recirculated via the HEPA filters vs direct in (hazardous drug compounding due to external venting requirement)

Image KPL

ROOM LAYOUT



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Challenges

- HEPA filters do not capture gases, VOCs or particles < 0.3 microns
  - Placement, air velocity, sealed ceiling tiles/door gaskets
  - Fans needed to drive air velocity increase noise pollution
  - 24/7 operation increases electricity utilization

- Facility constraints
  - Retrofitting vs new construction
  - Conflicting requirements between DPH/fire/life safety/security construction requirements and cleanroom requirements
  - Environmental sustainability goals vs sterility measures
  - Cost and space

Challenges

- The chemicals we use to disinfect the hoods and rooms are extremely corrosive (e.g. Quaternary oxidizers, sporicidals) leading to VOCs, rust and delamination of surfaces
  - Rust particles are ~ 10 microns

- What effect do toxic gases and particulate matter have on sterile compounds? (Nitrogen dioxide, CO, ozone, sulfur dioxide)
  - pH changes can adversely affect stability
  - Filtering is generally reserved for glass particles from ampules (5 micron filter), potential incompatibilities (0.2 micron filter) and less commonly terminal sterilization
  - Visualization is fraught with human error and vision constraints, can only detect large particles

Future Solutions

- **Research needed**
  - Effect of VOCs and non-viable particle contamination in sterile parenteral compounds – pH, solubility, toxic compounds, etc
  - Human health risks from parenteral sterile products contaminated with VOCs and non-viable particles
    - Anaphylaxis, occlusion of small capillaries, tissue infarction, granulomas, phlebitis, aveolar damage, death
    - Complicated as there are over 200 chemicals detectable in bodily fluids
  - Occupational exposure risk

Future Solutions

- **Regulations**
  - USP standards that define high risk non-viable particle contamination and mitigation strategies
  - Harmonization of various state Board of Pharmacy requirements above the USP requirements
  - Cleanroom construction standards
  - Public reporting of VOCs, toxic gases and particulate matter; CMS? EPA?

- **Monitoring**
  - Real time, continuous monitoring for elevated particle counts
    - Identification of contaminants
    - Elimination of contaminants

References

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