

The ABCs of VOCs

Basic Science to Precision Understanding

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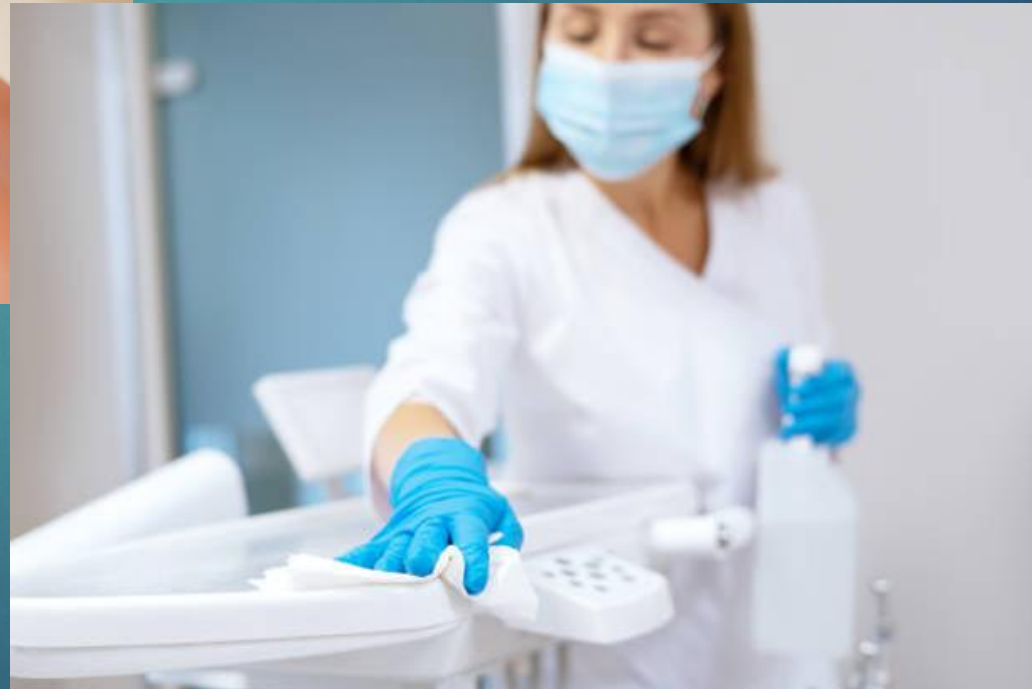


Case Study: VOCs in the IVF Lab



“VOCs cannot cross from the air into my culture dish, right? Maybe? I hope?”

We wish...



Things I hear all the time...

- ▶ We don't use alcohol, therefore there cannot be any alcohol in our lab!
 - ▶ **What about your neighbors?**
 - ▶ **Russack et. al. 2025: IPA present at high levels in over 50% of IVF labs**
- ▶ We have positive pressure and lots of air changes – we are fine!
 - ▶ **What kind of air are you bringing in?**
- ▶ We change out our filters often – we cannot be harmed!
 - ▶ **What types of filters? And where are they?**

Topics of Discussion

▶ **Background: Indoor Air Quality (IAQ) in IVF**

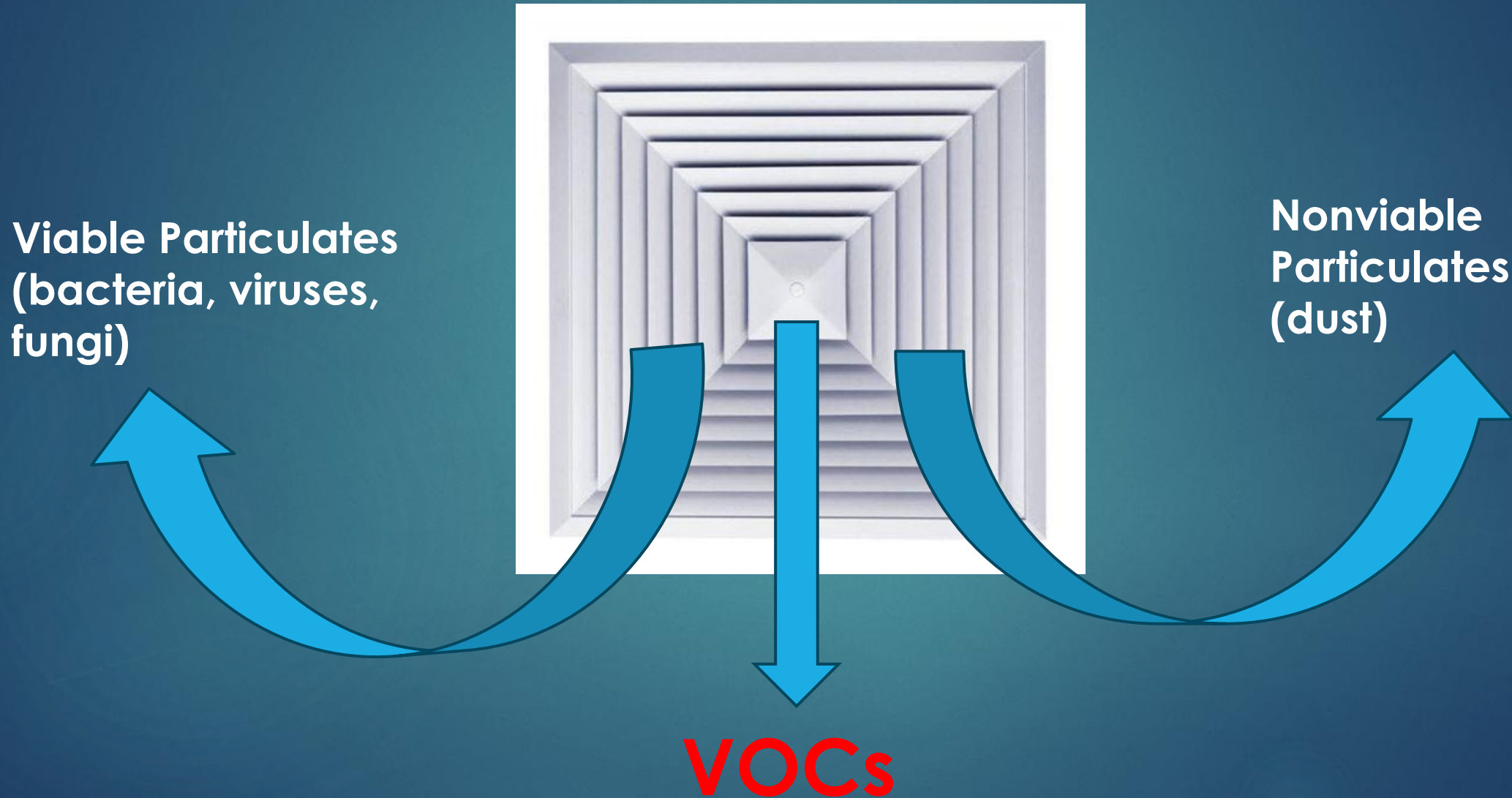
- ▶ What is a VOC? And why should I care?
- ▶ What factors influence my air quality?

▶ **A Deeper Dive: Important Properties**

- ▶ How different VOCs differ in impact...
- ▶ How do these VOCs carry out unwanted effects?

▶ **Takeaways: Reductions, what you can do... data + action**

“Three Variables of Air”: IAQ



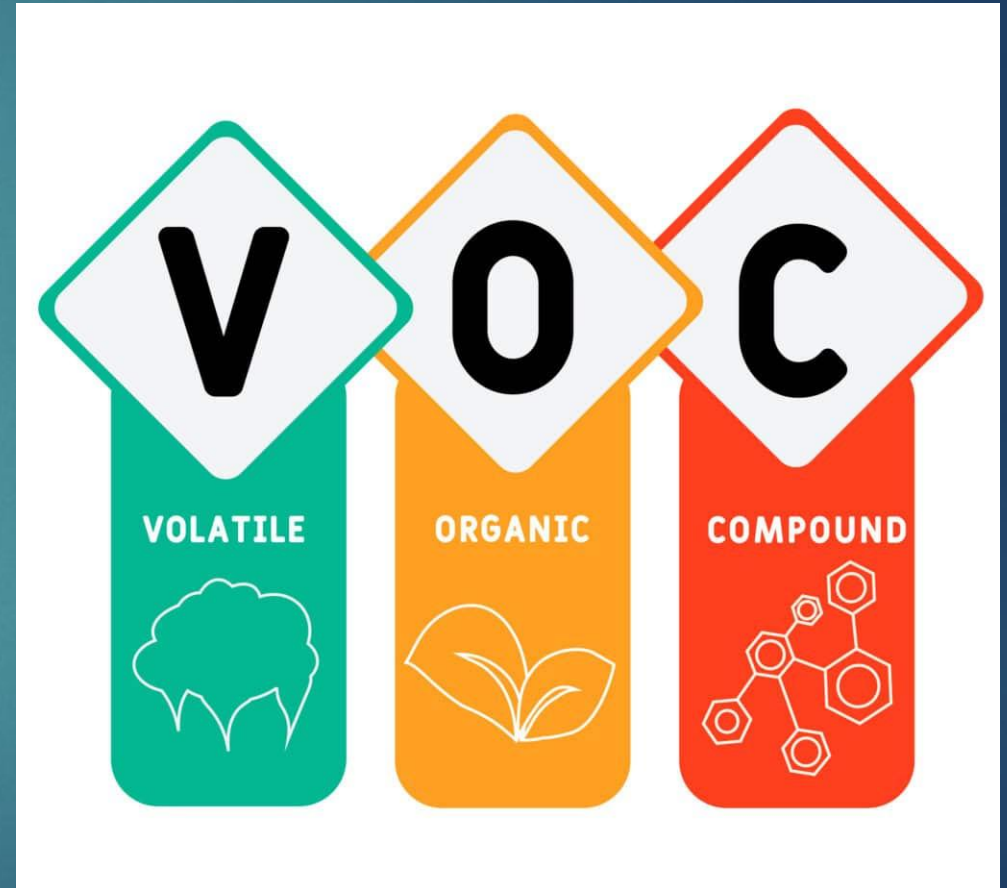
What Are VOCs? What Aren't VOCs?

Volatile Organic Compounds (VOCs)...

- ▶ Volatilize into air space, cause odor
- ▶ LOW boiling point, HIGH vapor pressure
- ▶ Indoor concentrations **2-10x** outdoor (Up to 1000x)

Does not include...

- ▶ NH_3 , CO , CO_2 , H_2O_2 (+ other inorganics!)
- ▶ Quarternary Ammonium (Quats, QACs)
- ▶ Dust (unless the dust shuttles in VOCs)



Indoor Sources: VOCs Common to the IVF Lab

- ▶ Cleaning products
- ▶ Laboratory equipment
- ▶ Containerized gas
- ▶ Building materials
- ▶ THE EMBRYOLOGIST
 - ▶ Personal care products
 - ▶ Hand sanitizers
 - ▶ Detergents



Outdoor Sources: VOCs Common to the IVF Lab

- ▶ Fires
- ▶ Automobile exhaust
- ▶ Construction
- ▶ Seasonal fluctuations
- ▶ Industrial impacts

**AUDIENCE: WHAT ELSE AM
I MISSING?**



Profiling VOCs in IVF

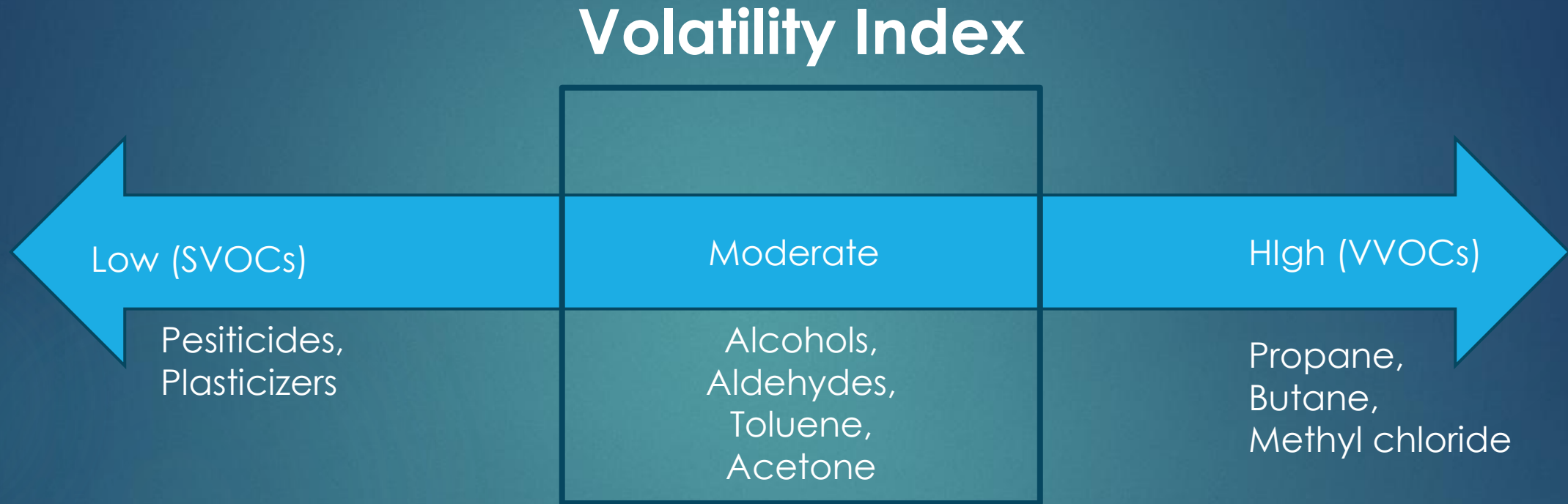


- 90,000+ VOCs (EPA)
- Each VOC has its own “fingerprint”
 - unique partition coefficient
 - level of hydrophobicity
 - vapor pressure.
- Once present in media, VOCs are **thermodynamically fixed** in the culture environment.



STEP 1: VOC leaves the air,
enters the culture dish.

Chemical Classifications: Volatility



***Molecular weight:**

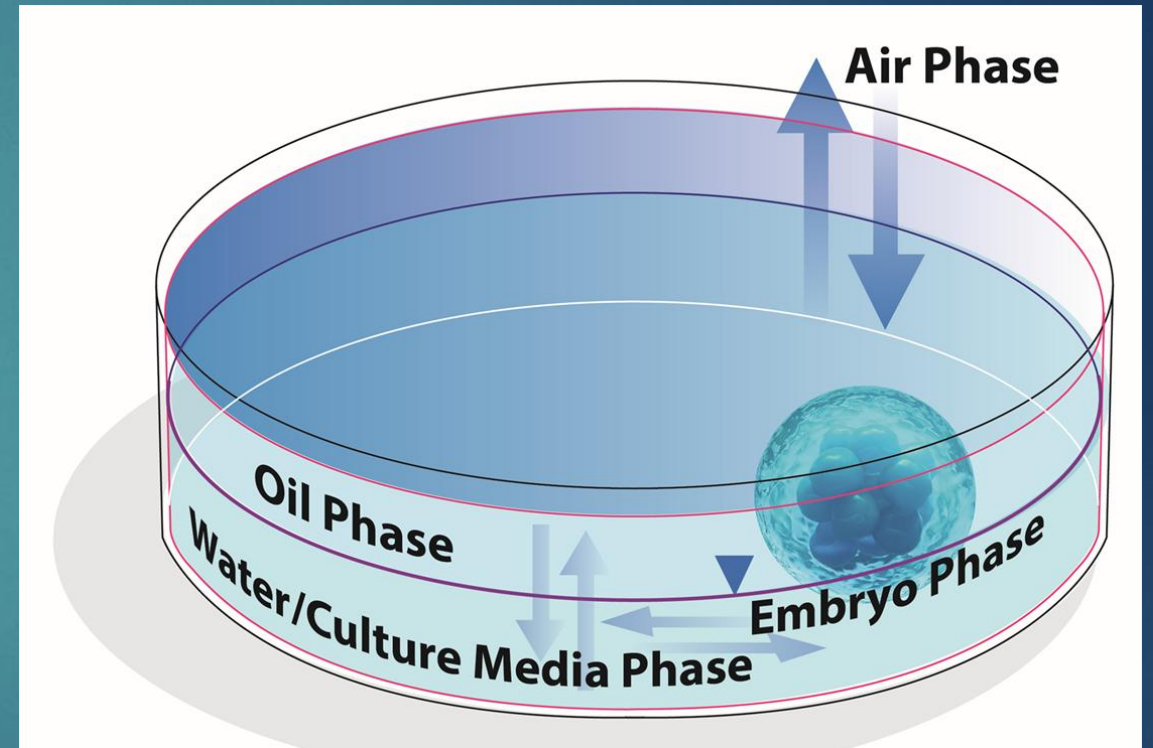
- ▶ impacts removal efficiency
- ▶ Impacts how quickly VOCs migrate



STEP 2: VOC “partitions”
between oil, media, embryo...

Equilibrium Partitioning Modeling

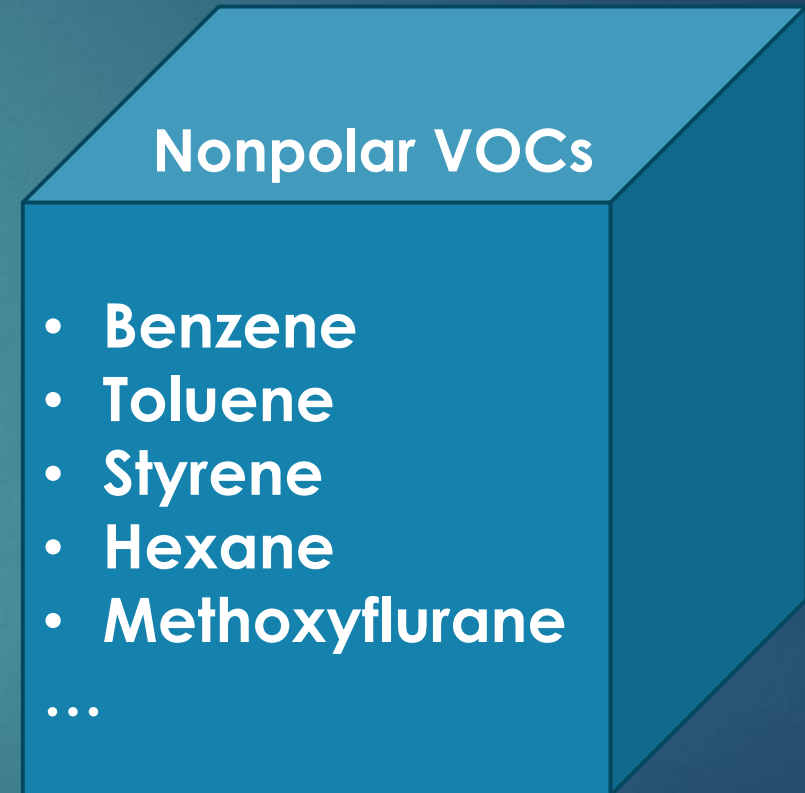
- ▶ At equilibrium, VOCs partition across phase boundaries – described by partition coefficients
- ▶ Airborne concentration → oil → media → embryo



Chemical Classifications: Polarity



Affinity for: Water-based culture media, humidity droplets in the air



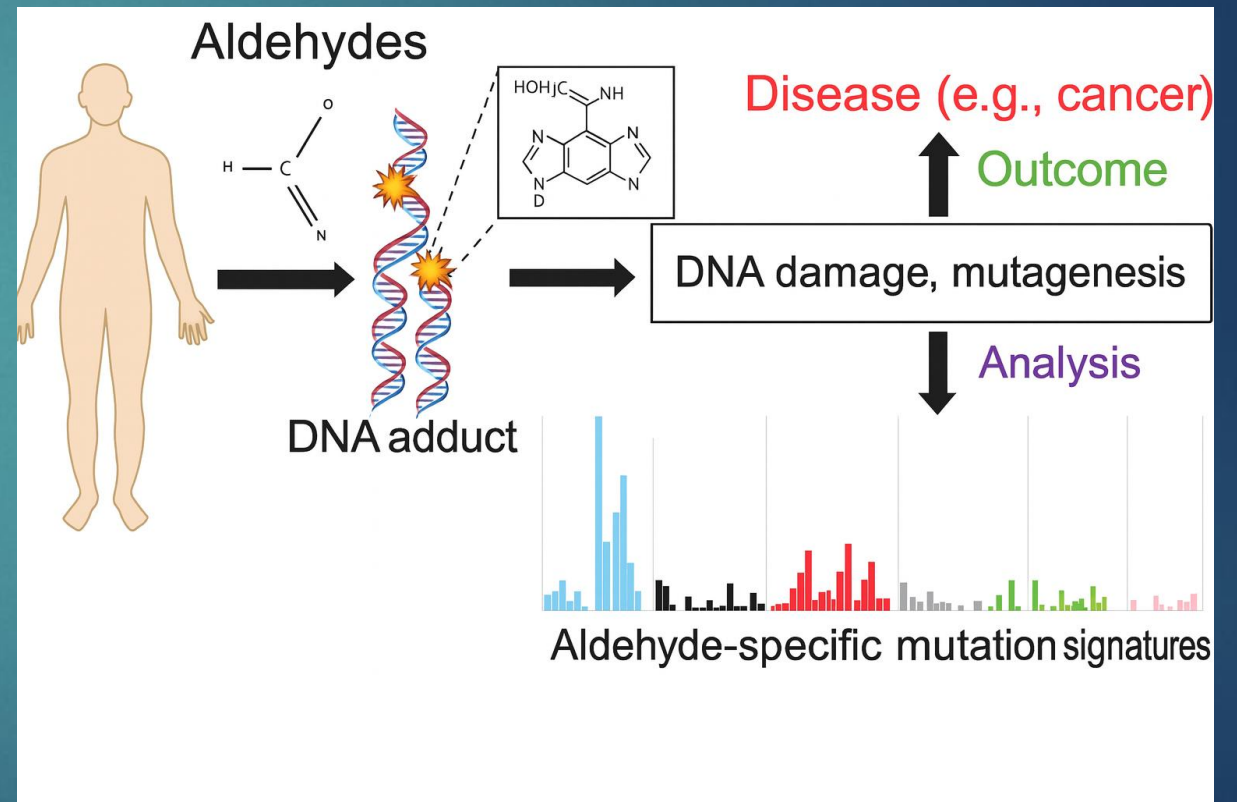
Affinity for: Oil overlay, biological matter (lipids/proteins)

STEP 3: Toxicity ensues!



Cellular and Subcellular Impacts of VOC Exposure: What Do We Know?

Animal models and human cell experiments



Impact of VOCs on Cell Metrics and Embryo Delivery to Patient

- ▶ Decreased cell culture metrics – reduced growth, cell viability
- ▶ Decreased cell potential
- ▶ Increased cell loss
- ▶ **Increased clinical failure** (Cohen et al, 1997, Hall et al, 1998, Mayer et al, 1999, Boone et al, 1999, Worrilow et al, 2001, Worrilow et al, 2002, Esteves et al, 2004, Knaggs et al, 2007, Merton et al, 2007, Esteves et al, 2013, Hang et al, 2013, Forman et al, 2014, Munch et al, 2015, Heitmann et al, 2015, Worrilow et al, 2016, Palter et al, 2016)

Cairo Consensus

- ▶ **Cairo Consensus (2018):** best practices guide for IAQ
 - ▶ Recommendations for building materials, workstation, gas systems, layout
 - ▶ 60 VOCs profiled in “older style” and “modern” labs, as well as total levels (TVOCs)
- ▶ **Cairo Consensus recommendations:** $<500 \mu\text{g}/\text{m}^3$ TVOCs (400-800 ppb), $<5 \mu\text{g}/\text{m}^3$ aldehydes
 - ▶ No other species-specific thresholds...

How Much??

What the heck is IVF?

“Alle Ding sind Gift und nichts ohn’ Gift; allein die Dosis macht, das ein Ding kein Gift ist”

“The dose makes the poison”

-Paracelsus, 1538



Looking at Individual VOCs...

Different Critical Concentrations

- ▶ Alcohols: lower than Cairo Consensus
 - ▶ **Example: IPA: 32.2 ppb airborne is the modeled toxic level!**
- ▶ Some more volatile species: may be higher than Cairo Consensus

Variables of importance: temperature, time of exposure, surface area of exposure

How Fast?? (Characteristic Time)



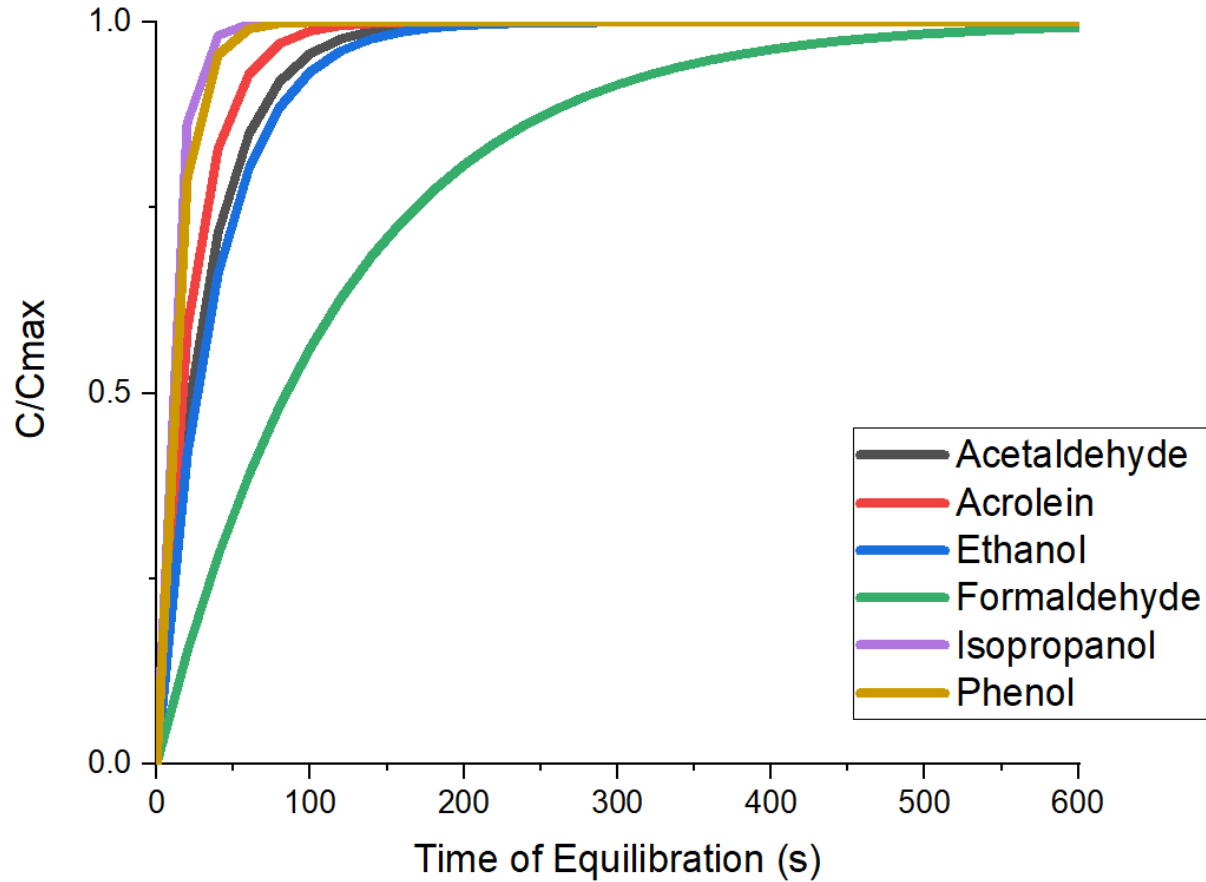
Eliud Kipchoge, 1:59:40 marathon, Vienna, Austria (2019)



Usain Bolt, 9.58 s 100 m, Berlin, Germany (2009)

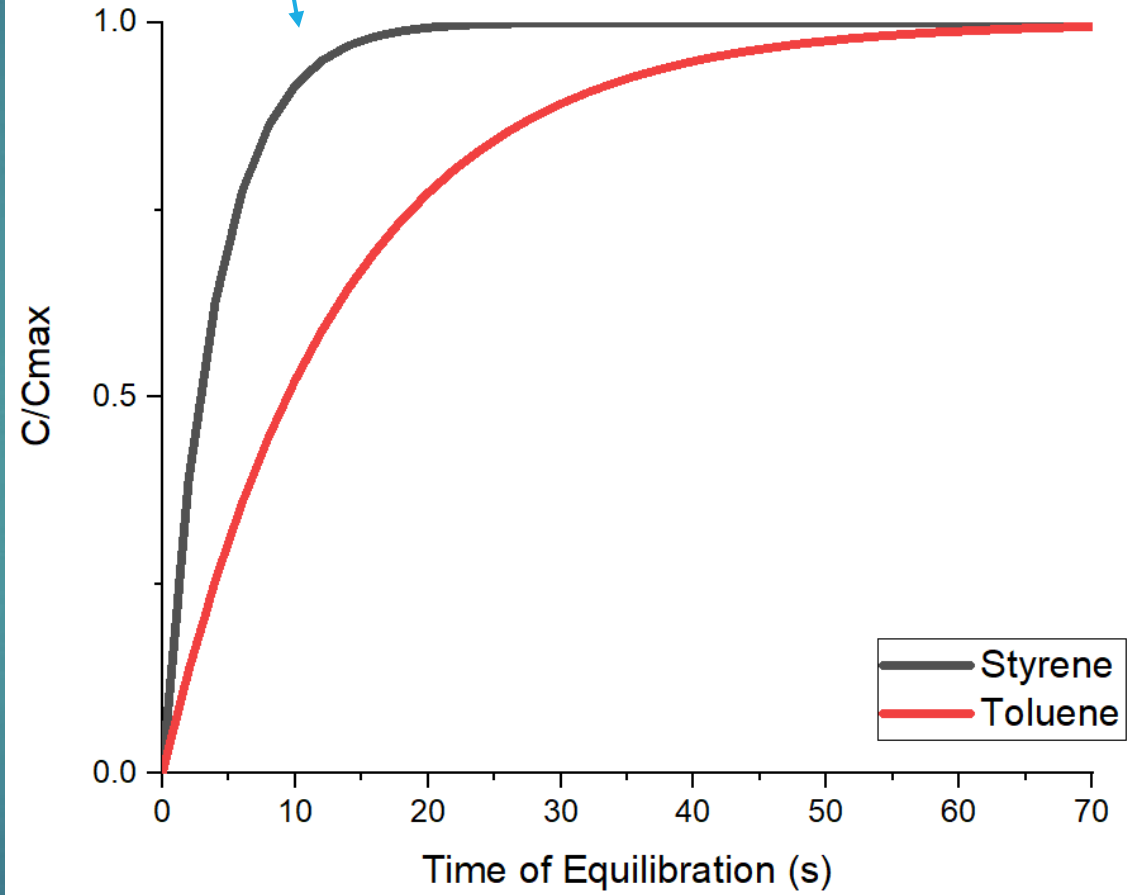
Kinetic Modeling: How Fast?

Hundreds of seconds (a few minutes)



Polar species

Tens of seconds (less than 1 minute)



Nonpolar species

Ongoing Research

▶ **Duke University / LifeAire Systems**

- ▶ Once the VOC has entered the culture media, what impacts occur? How do different VOCs differ?
- ▶ Investigating oxidative stress, senescence, morphokinetics, transcriptomics...
 - ▶ **Specific mechanisms?**
 - ▶ **Cellular and Clinical Impacts?**



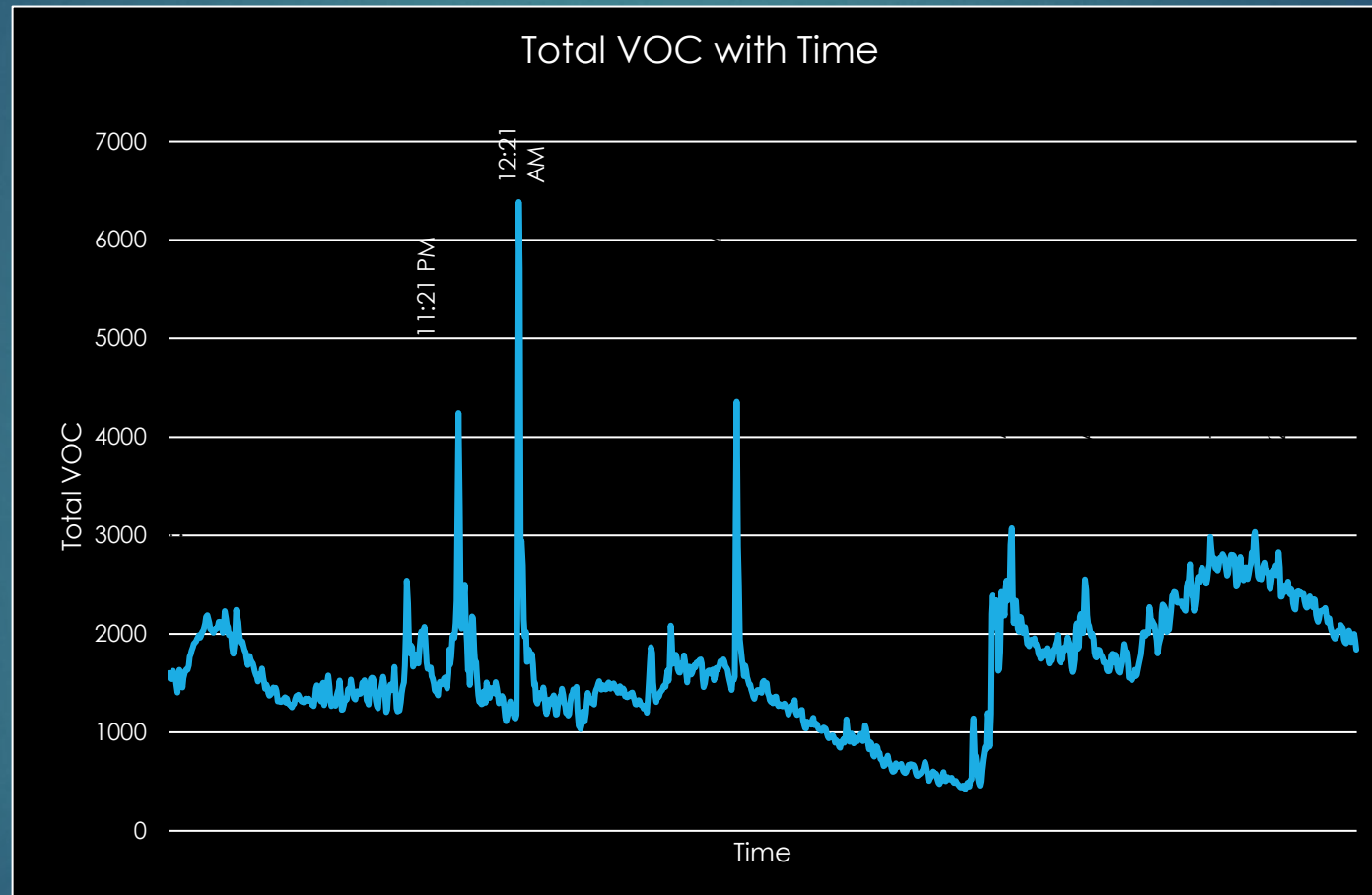


Actionable takeaways:

IDENTIFY + REMEDIATE

**So.....What does this all mean?
How can you approach air quality data?**

Methods of VOC Detection: Photoionization (PID)



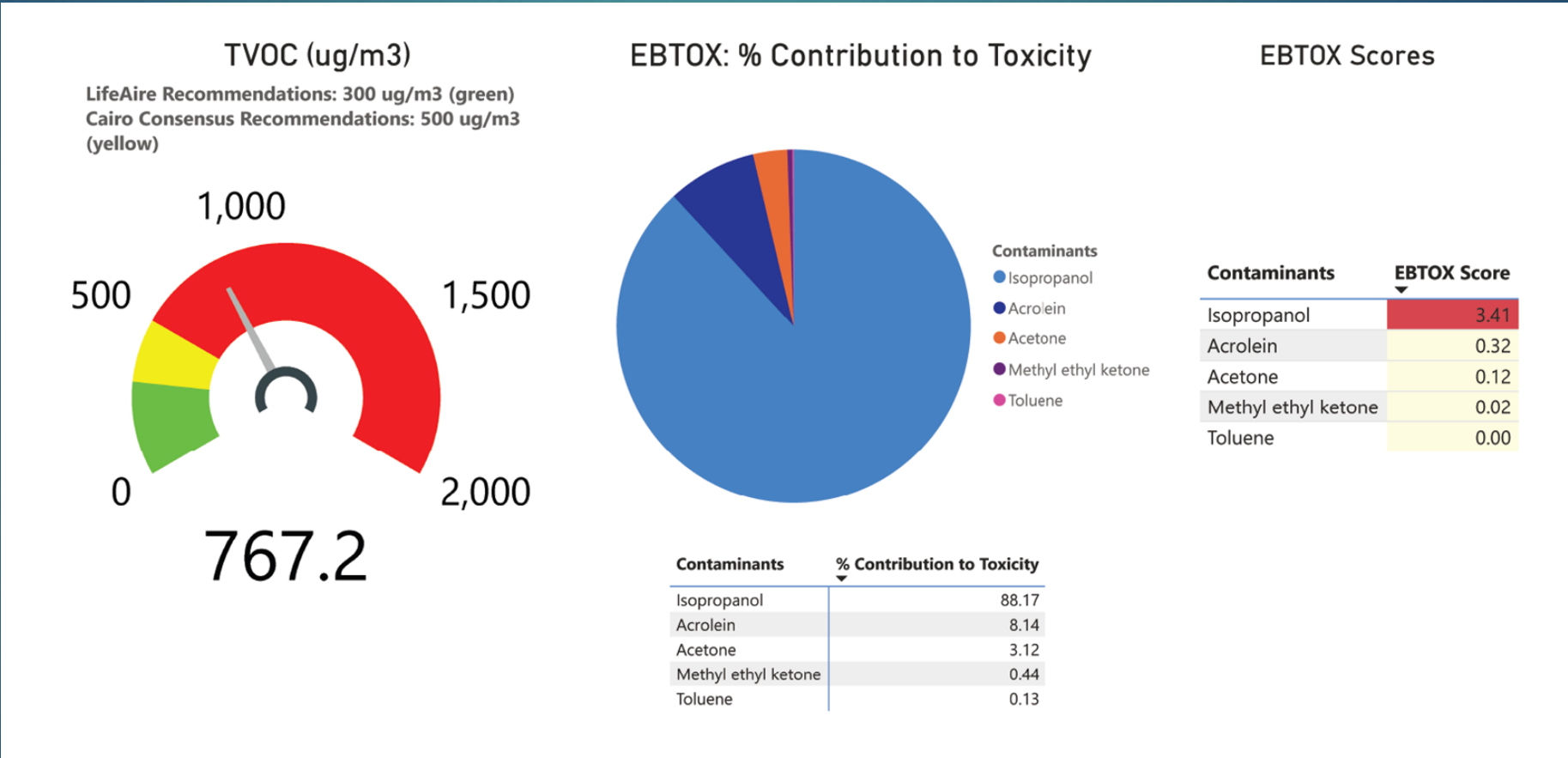
“How, exactly, does my overall VOC load change with time?”

Methods of VOC Detection: EPA Canister Methods



**“What, exactly,
is the
composition of
my air?”**

Embryonic Burden and Toxicity Scale (EBTOX[®])



When Should I Test?

- ▶ Odor present in the lab
- ▶ Decreased clinical metrics
- ▶ Nearby environmental event
- ▶ Nearby construction
- ▶ Random or scheduled check in
 - ▶ **Invisible threats!**

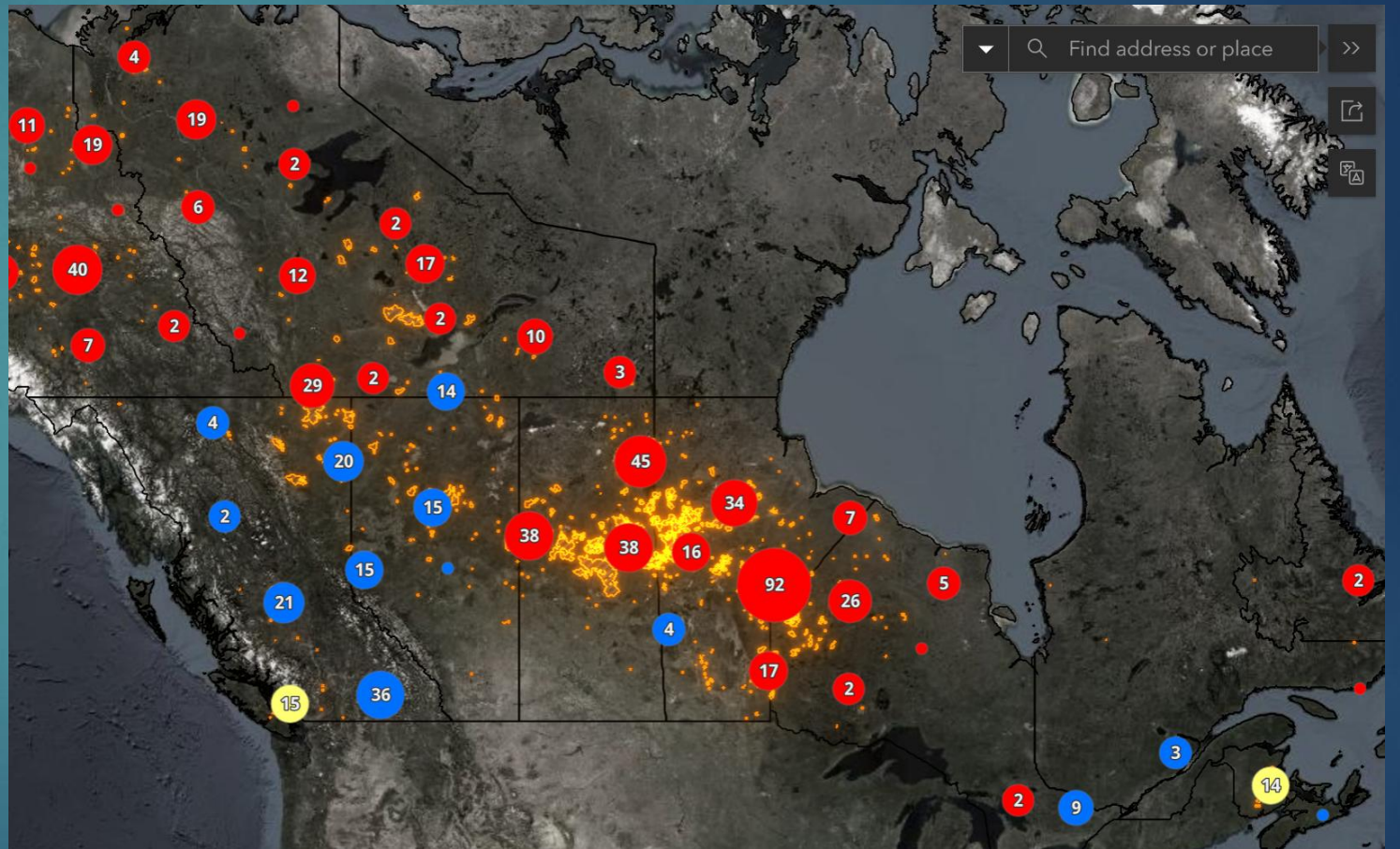


Figure: <https://climate.esri.ca/pages/wildfire>

Conclusions

VOCs enter the cell culture from the ambient air and cause complex responses that may severely impact patient outcomes.

- ▶ VOCs are not “one size fits all”!
- ▶ Different chemical and physical properties lead to different biological endpoints
- ▶ Difficult to “outrun” airborne VOCs: best bet is to prevent them being present in the first place!
- ▶ EPA Method testing + accurate PID testing = best IAQ data

The ABCs of VOCs

From Basic Science to Precision Understanding

Thank you!

(References available upon request)



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