



The Role of Detection in Biodefense

2003 New England Bioterrorism Preparedness Workshop

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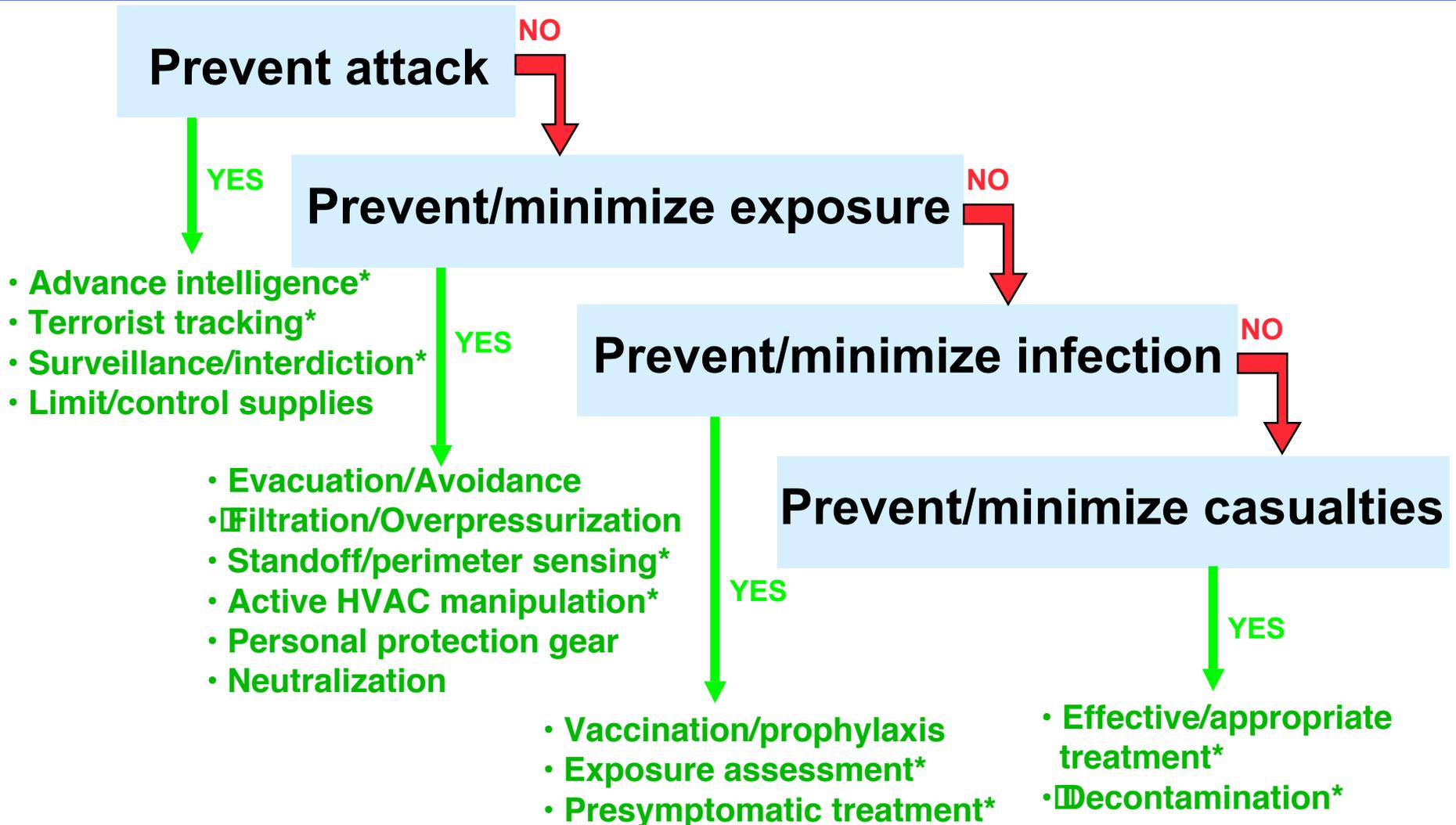
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Overall Biodefense Strategy



* Detection required

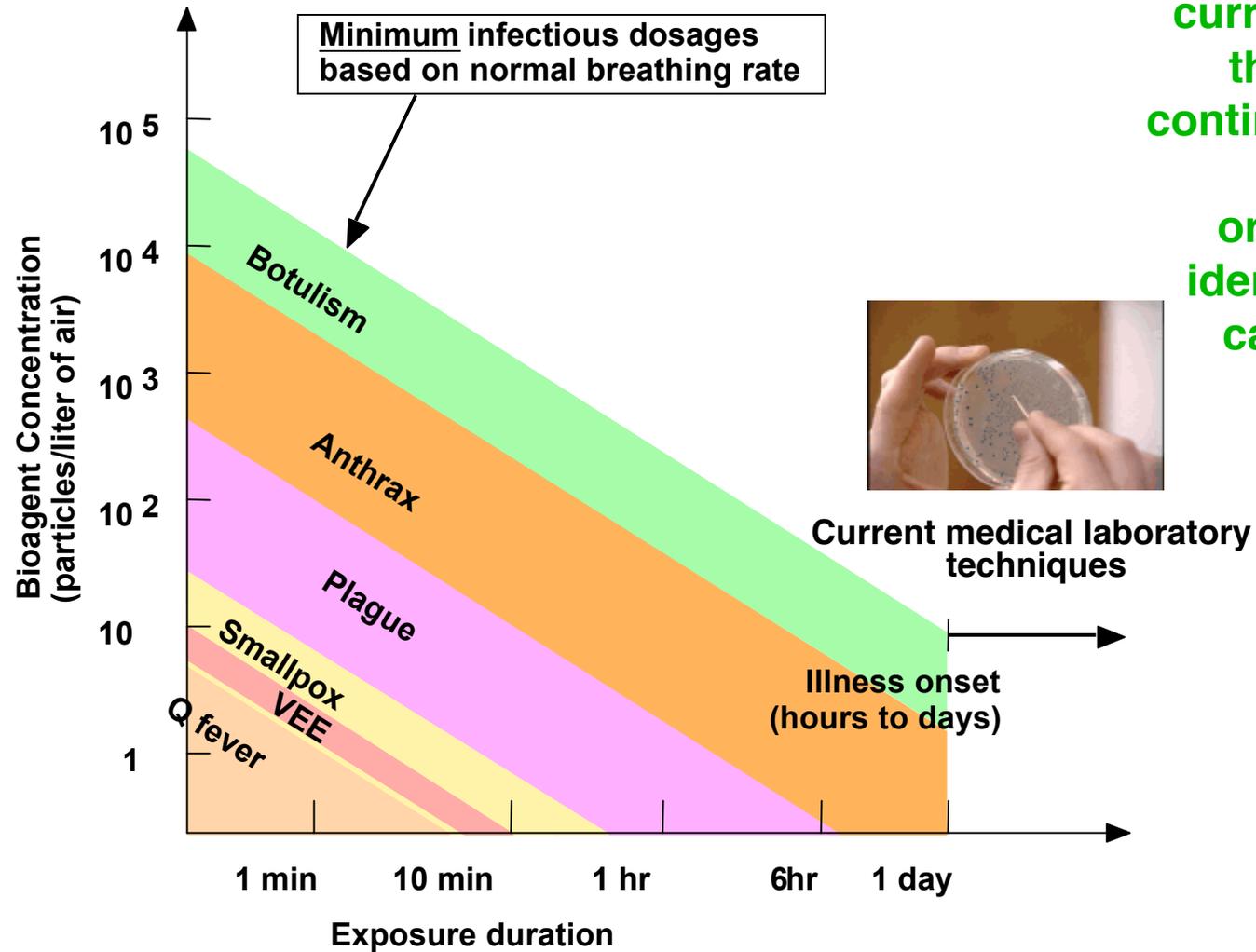


The Challenge of Biological Agent Detection

- **Protection requires rapid detection of pathogens in the environment (no false negatives, few false positives)**
- **Treatment and retaliation require accurate determination of the agent and its source**
- **Why is this so difficult?**
 - **Even low concentrations can be lethal**
 - **Aerosol are small (1 - 10 microns)**
 - Low scattering cross section
 - **Signatures can be non-specific**
 - Very different from chemical agents
 - **Biological technologies widespread that may mask signature**
 - **Competing backgrounds**
 - Natural and man-induced substances
 - Indigenous bioaerosol, including pathogens



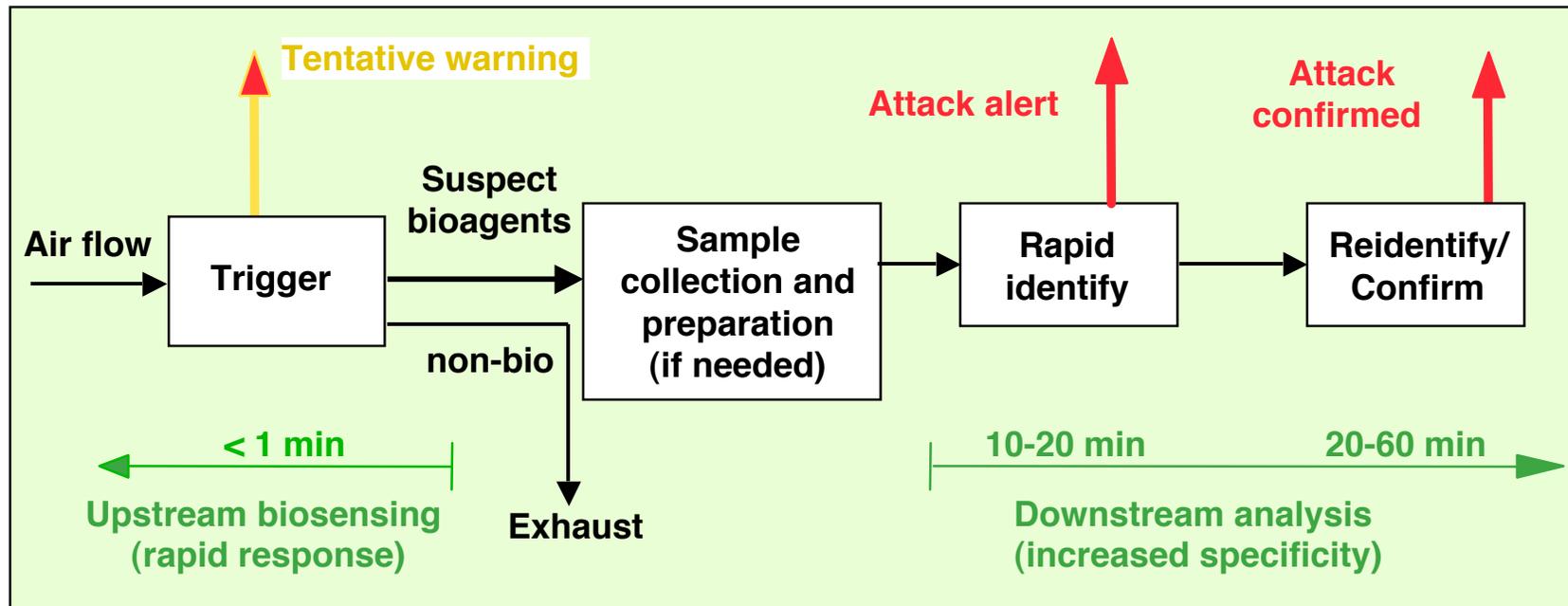
Sensing Requirements Driven by Understanding of Infectious Dosage



No sensing systems currently exist that offer continuous, real-time organism-identification capability



Generic Biosensor Architecture



- Particle count/sizing
- UV Laser-induced-fluorescence
 - Point
 - Standoff

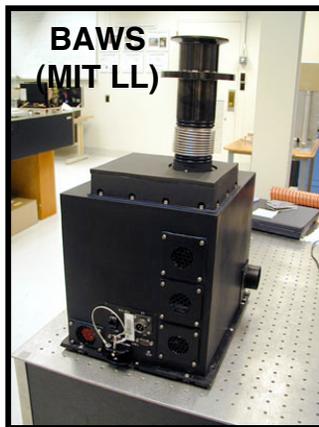
- Air-to-liquid collection
- Impaction
- Electrostatic separation

- Culture
- Immunoassay
- Cell-based
- PCR/DNA based
- Mass Spectrometry



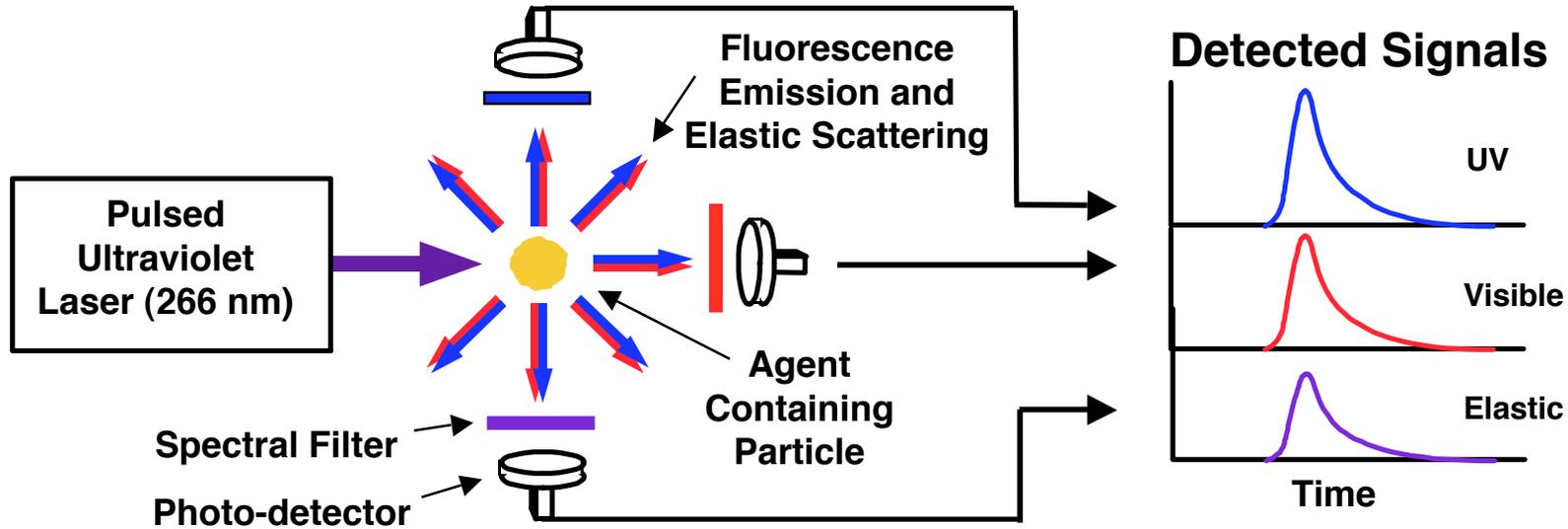
Examples of Trigger Sensing Technologies

- **Particle counting/sizing**
 - Simple, inexpensive, portable
 - Not specific to biologicals
- **UV Laser-Induced Fluorescence**
 - Offers biologic/nonbiologic differentiation
 - Has been developed for both point and standoff sensing

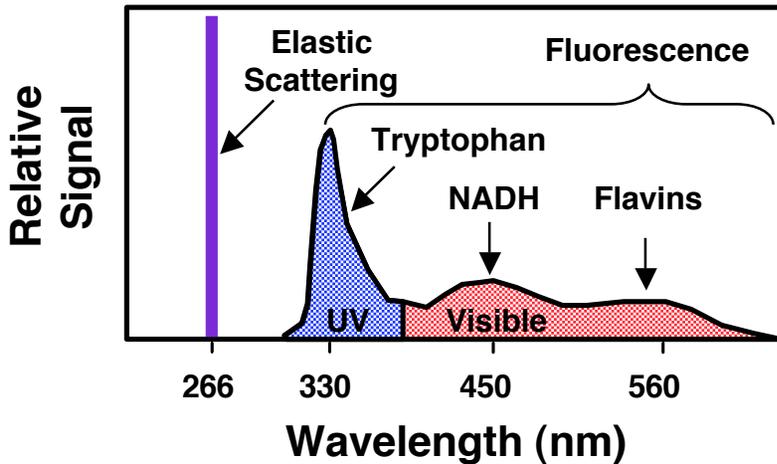




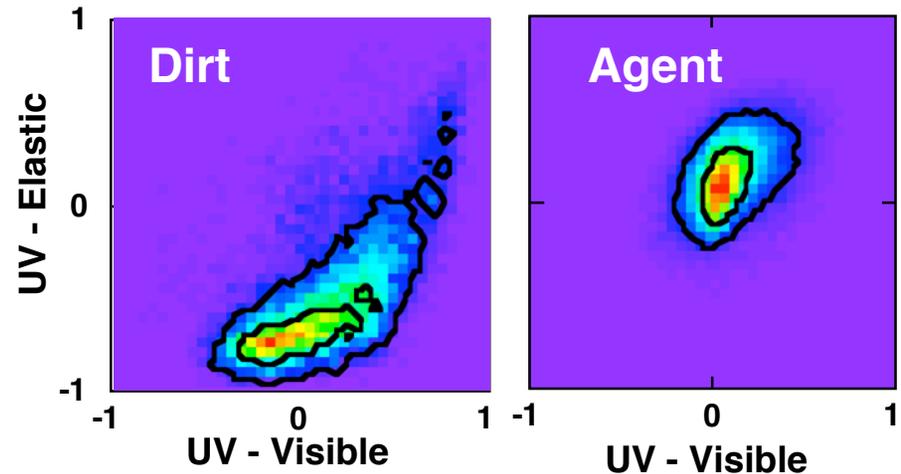
BAWS Principle of Operation



Particle Emission Spectrum



Particle Discrimination





Example of BAWS Response to Simulant Releases

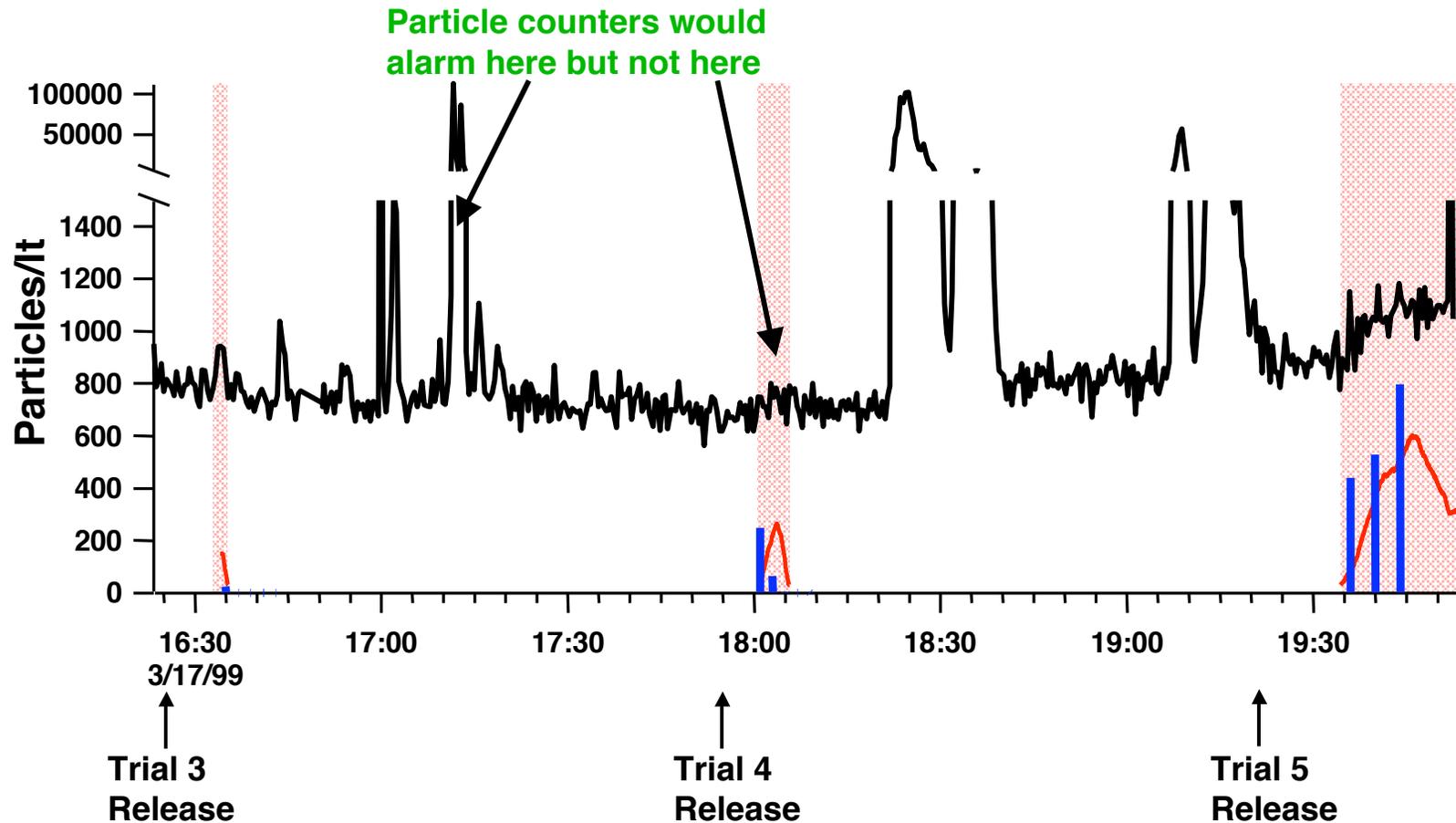
March 17, 1999
Dugway PreBLWE

Referee Data

- 2 - 10 μm particles (TSI APS)
- *Bacillus globigii* (STA sampler)

BAWS III Data

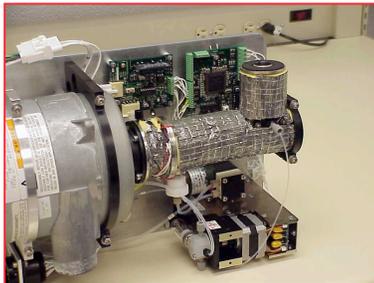
- Alarm window
- Agent





Collection of a Sample Following a Trigger

Air-Liquid Collection



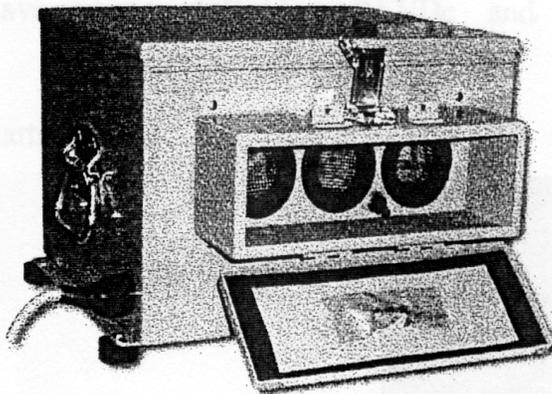
Wetted Wall Cyclone
(Battelle)



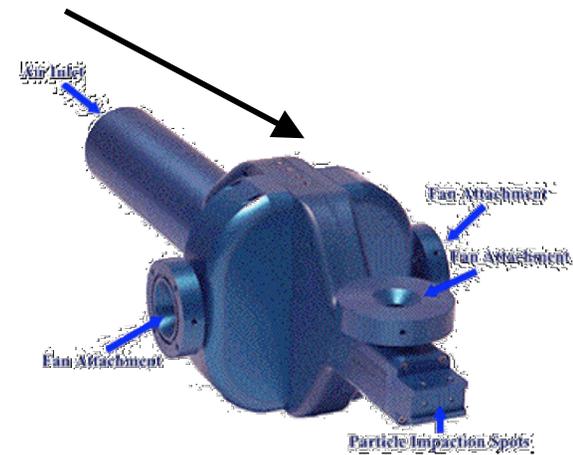
SpinCon (MRI)

- Collection systems can also be used for continuous monitoring
 - Periodic sampling and assay offers detect-to-treat for many threat agents

Dry Impaction



Dry Filter Unit



BioVic (MesoSystems)



Current Bioagent-Identification Technologies



Rapid ID

Immunoassays

Bioagent
Antibody
Labeled Antibody
Substrate

- Selectivity from high affinity binding of antibody to agent-specific structures

Orthogonal ID Confirmation Technologies

Polymerase Chain Reaction (PCR)

Chemical multiplication of DNA
($\times 10^6$)

Culture-based assays

- Selectivity from sequence-specific DNA/RNA recognition
- Enzymatic amplification provides superb sensitivity

- Traditional method since Pasteur – still “gold standard” for ID
- Viable organisms replicated in culture and identified using biochemical assays and microscopy





Examples of In-Use Rapid Identification Techniques



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**Ticket cartridges and reader
for lateral-flow immunoassay
in Joint Biological Point Detection System
(JBPDS)**



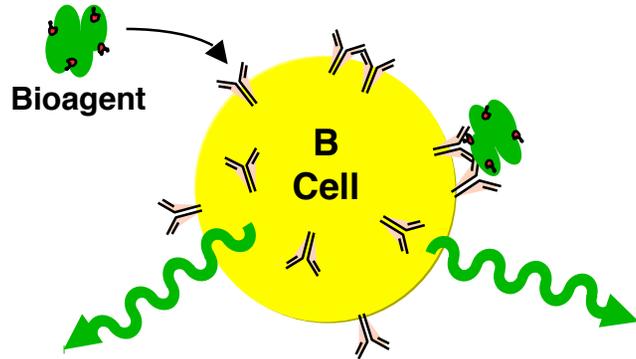
**Commercially available LFI tickets
and reader
(Tetracore/Alexeter)**

- **Immunoassay-based tickets are relatively fast and require minimal sample preparation but their sensitivity is often poor and readout fairly subjective for low concentrations**



Developmental Bioagent-ID Sensor: CANARY (DARPA/MIT LL)

Concept

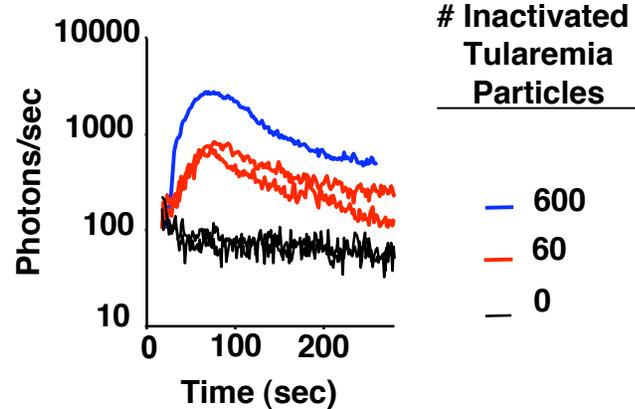


B cell emits ~200 photons within
30 seconds after bioagent binding

Prototype microcentrifuge device



Tests Against Killed Tularemia (Collab. with NMRC)





Confirmation Identification Technology

- **Systems being developed (and deployed) that provide agent ID within 30 minutes of introduction of prepared sample**
- **Challenge remains in automating sample preparation and analysis**

Semi-automated field-portable
PCR devices



RAPID - Idaho Technologies



*SmartCycler
XC System - Cepheid*

Example of handheld PCR
device



Bioseq - Smiths



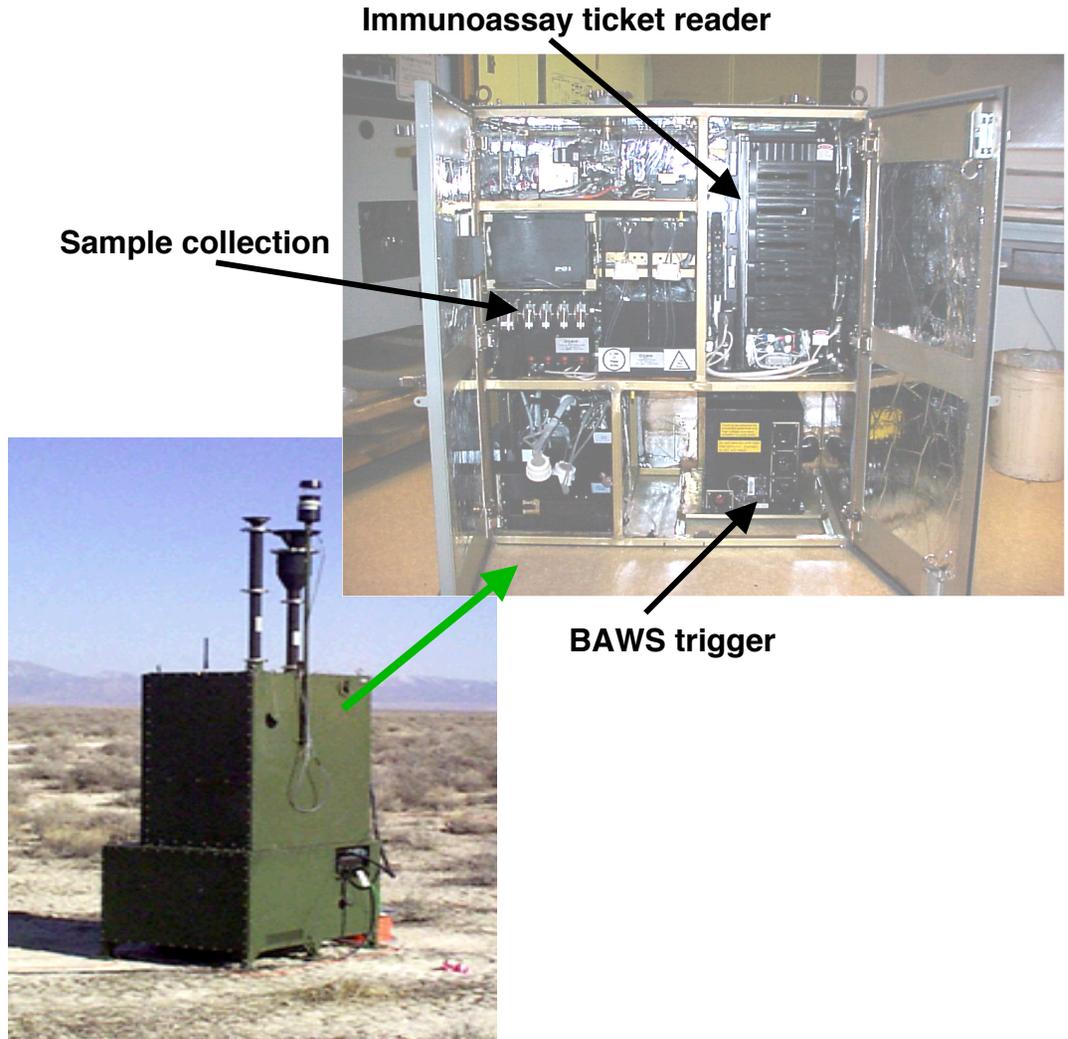
Examples of Integrated Systems



**Biological Integrated
Detection System (BIDS)**



Portal Shield



**Joint Biological Point
Detection System (JBPDS)**



Military versus Civilian Detection Systems

- **Military systems developed primarily for outdoor force protection**
 - Emphasis has been on preserving functionality during assault (i.e., put masks on) and minimizing exposure (avoidance)
- **Technology limitations on real-time detection and identification have driven users to multi-stage architectures**
 - Fast non-specific trigger sensors followed by sample collection and multi-tiered assay
- **Civilian Biodefense can borrow from military investment but requirements do differ**
 - The most successful technologies will offer benefits above and beyond those given by Biowarfare protection (e.g., better infectious disease control, early diagnostics, exposure assessment, treatment, etc.)