# **CDC PUBLIC HEALTH GRAND ROUNDS**

# Strengthening a Culture of Laboratory Safety



#### December 15, 2015



U.S. Department of Health and Human Services Centers for Disease Control and Prevention

## **Evolution of Laboratory Safety Standards**



### Steve Monroe, PhD

Associate Director for Laboratory Science and Safety Centers for Disease Control and Prevention



U.S. Department of Health and Human Services Centers for Disease Control and Prevention

## **Origins of Laboratory Science at CDC**

- **1942** Malaria Control in War Areas
- **1943 Communicable Disease Center**
- **1970** Center for Disease Control
- **1992** Centers for Disease Control and Prevention



Dr. Joseph W. Mountin



Class of state laboratory personnel at the Communicable Disease Center

# **Current Scope of Laboratory Science at CDC**

## **CDC's laboratory work now includes:**

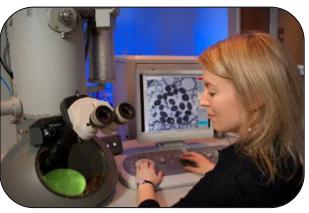
- Infectious diseases
- Noninfectious diseases
- Environmental health
- Occupational health
- Laboratory systems (e.g. standards, quality guidelines)



Viral Special Pathogens Branch



Tobacco and Volatiles Branch



Infectious Diseases Pathology Branch

# **Current Scope of Laboratory Science at CDC**

- Outbreak investigations
- Emergency response
- Population health studies
- Laboratory quality improvement
- Advanced Molecular Detection

- Genetic studies
- Biomonitoring
- Vaccine development
- **Pathogen discovery**
- Newborn screening



The National Institute for Occupational Safety and Health

5



Poxvirus and Rabies Branch



Newborn Screening and Molecular Biology Branch

#### **Over 2,000 laboratory staff**



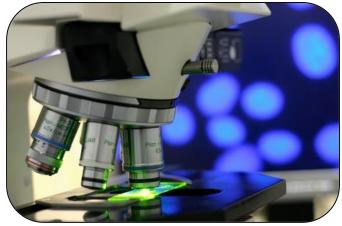
## Laboratory Staff

- Biologists
- Chemists
- Veterinarians
- Engineers
- Medical technologists
- Biosafety experts
- Quality managers

#### **Over 2,000 laboratory staff**



#### **Over 150 laboratory groups**



## **Biosafety Level (BSL)**

### BSL-1:

Low potential of disease and risk to environment

#### BSL-2:

Moderate potential of disease and risk to environment

### **BSL-3**:

Serious or potentially lethal disease after inhalation

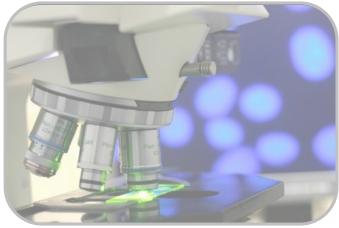
### □ BSL-4:

High risk of disease through aerosol exposure, causing severe to fatal illness with no vaccine or treatment available

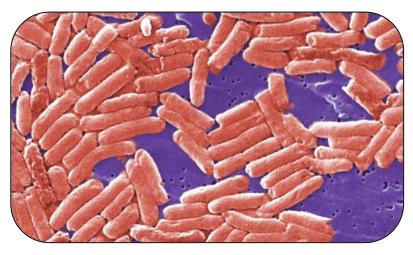
#### **Over 2,000 laboratory staff**



#### **Over 150 laboratory groups**



#### **Over 200 infectious pathogens**



## Pathogens

- Viruses
- Bacteria
- Parasites
- 🕨 Fungi
- Prions (infectious agents composed of misfolded protein)

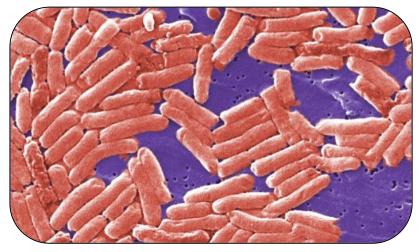
#### **Over 2,000 laboratory staff**



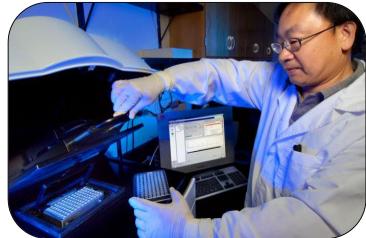
#### **Over 150 laboratory groups**



#### **Over 200 infectious pathogens**



#### Over 5,000 samples processed per day



PHIL ID 10032

## **Laboratory Safety Standard Evolution**

#### Safety standards change as new information becomes available



A scientist in 1943 works with potentially dangerous chemicals without modern personal protective equipment (PPE)



Two scientists in 1967 using practices no longer considered appropriate today

## **Laboratory Safety Standard Evolution**

### **Evolving Practices**



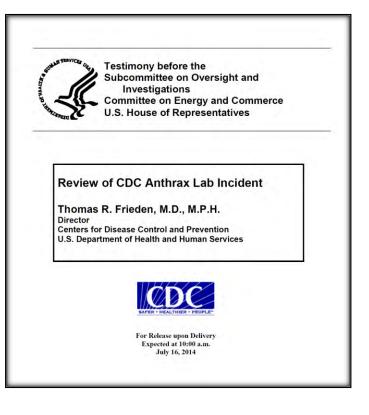
A scientist works with infectious influenza virus without modern personal protective equipment (PPE)

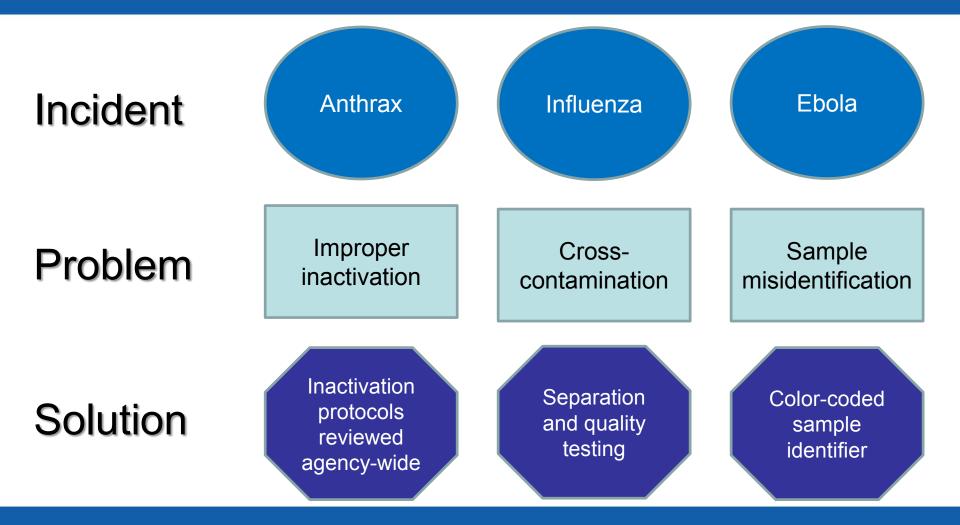


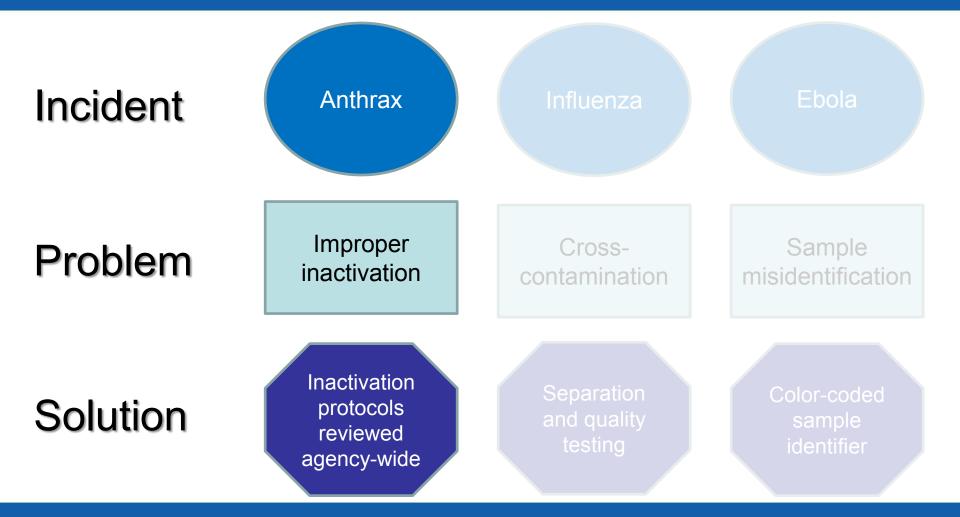
Today, scientists use biological safety cabinets (BSC) and powered air purifying respirators (PAPR) when working with highly pathogenic avian influenza virus

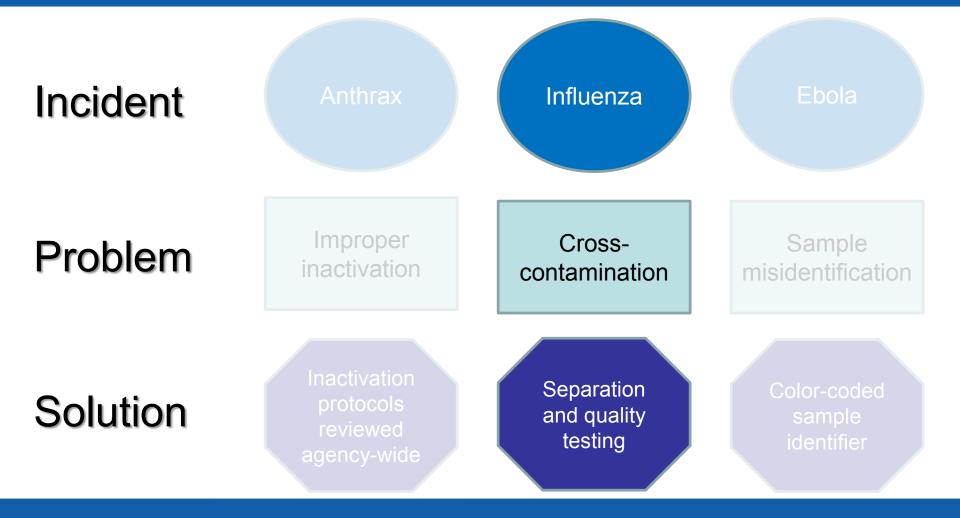
"What we're seeing is a pattern that we missed, and the pattern is an insufficient culture of safety."

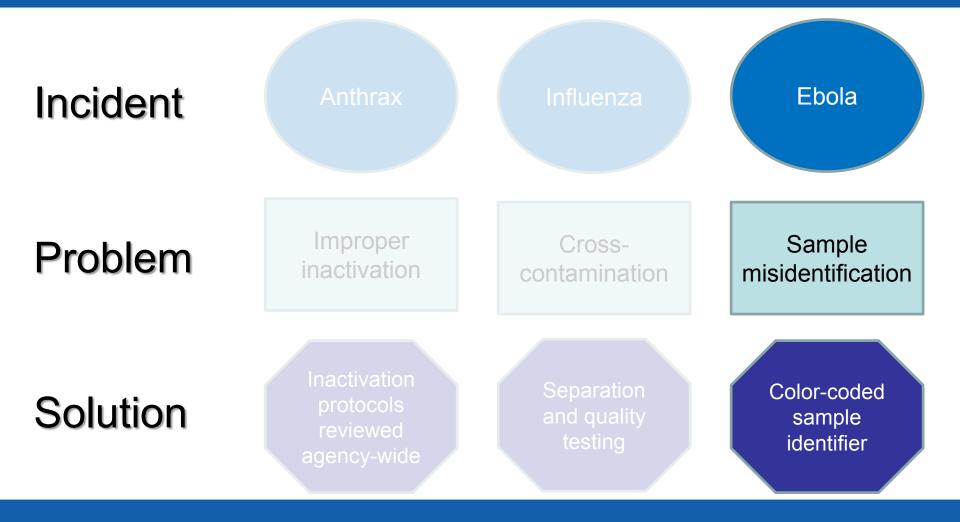
> Dr. Thomas Frieden, Director, CDC











# Changes Implemented at CDC in Response to External Review Findings

## **Established clear laboratory leadership**

- Provide scientific, technical, and managerial guidance to enhance science, safety and quality
- Advocate for laboratory science within the agency

## Revised laboratory competency training

Laboratory Safety Training Board to develop and update courses to support a standardized, competency based CDC curriculum

## Creating a "CDC Way" of performing risk assessments

- Pursuing external accreditation
  - Identify best practices for broad QMS implementation across CDC
- Clarified incident notification

cdc.gov/about/lab-safety/laboratory-safety-workgroup/workgroup.html QMS: Quality Management Systems

# **New Laboratory Science and Safety Leadership**

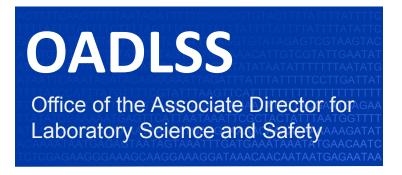
## Vision

Make CDC labs the gold standard for scientific excellence and safety

## **Goals**

- Leadership
- Policy and compliance
- Communication and collaboration
- Laboratory improvement
- Training





cdc.gov/about/lab-safety/index.html

# Laboratory Leadership Service

## Mission

Develop future public health laboratory leaders who integrate laboratory safety and quality as a principal standard of practice in every facet of their work

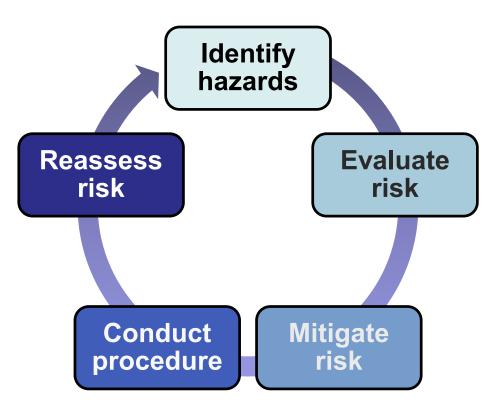
## Laboratory Leadership Service Principles

- Integrate safety and quality into laboratory science
- Provide training through service
- Promote applied public health laboratory research
- Produce future public health laboratory leaders



Inaugural LLS Fellowship Class of 2015

### **Risk Assessment Process**



## Before

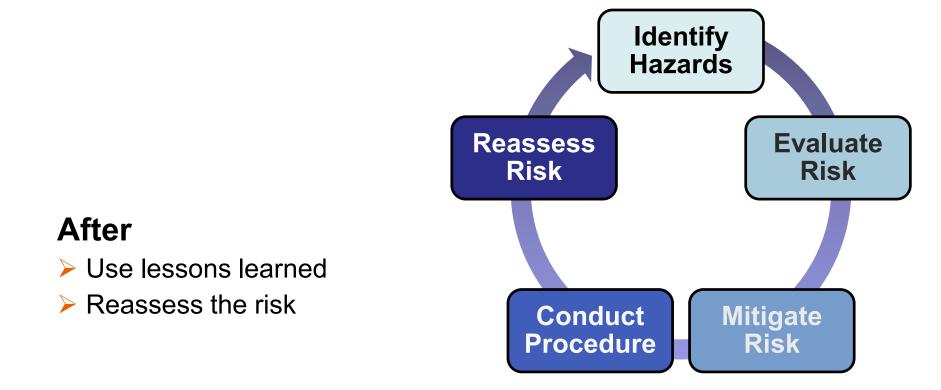
- Ensure research benefits outweigh the risks
- Explore safer alternatives
  - Use of non-pathogenic strains
- Predict potential problems



## During

- Have a contingency plan
- Prompt notification of incidents and near misses





## Before

- Ensure research benefits outweigh the risks
- Explore safer alternatives
  - Use of non-pathogenic strains
- Predict potential problems

## During

- Have a contingency plan
- Prompt notification of incidents and near misses

## After

- Use lessons learned
- Reassess the risk



## Conclusions

- Laboratories and lab scientists are essential to all aspects of public health
- **CDC** laboratories have a unique scope of work
- CDC laboratory science has the opportunity for improvement in safety and quality of work
- Risk assessment is critical at the agency, individual laboratory, and worker level

## Quality, Safety and Public Health Impact of Laboratory Science: A Case Study



## Conrad P. Quinn, PhD

Chief, Meningitis and Vaccine Preventable Diseases Branch Division of Bacterial Diseases National Center for Immunization and Respiratory Diseases Office of Infectious Diseases



U.S. Department of Health and Human Services Centers for Disease Control and Prevention

# The CDC Anthrax Vaccine Research Program: A Congressional Mandate

- Designed, managed, analyzed, and reported under CDC sponsored Investigational New Drug application
- Why CDC?
  - High public trust
  - No conflict of interest
  - Quality of science

#### Comprehensive and collaborative

- Laboratory scientists
- Clinical practitioners
- Statisticians
- Academics
- Interagency partners



# The CDC Anthrax Vaccine Research Program: A First for CDC

### Regulatory compliant

- Good Clinical Practice (cGCP)
- Good Laboratory
  Practice (cGLP)
- Quality assured laboratory data

### Data submission to FDA

- Manufacturer's supplemental BLA
- Basis for regulatory action



FDA: Food and Drug Administration BLA: Biologics License Application

# **The Laboratory Component**

#### Microbial Pathogenesis and Immune Response (MPIR) laboratory

- Established February 2001
- Laboratory support to AVRP
- To build human clinical trials capability
- Expertise of Anthrax disease development

#### Build and apply a customized QMS

CLIA, ISO-9000, 21 CFR Part 58, CDC

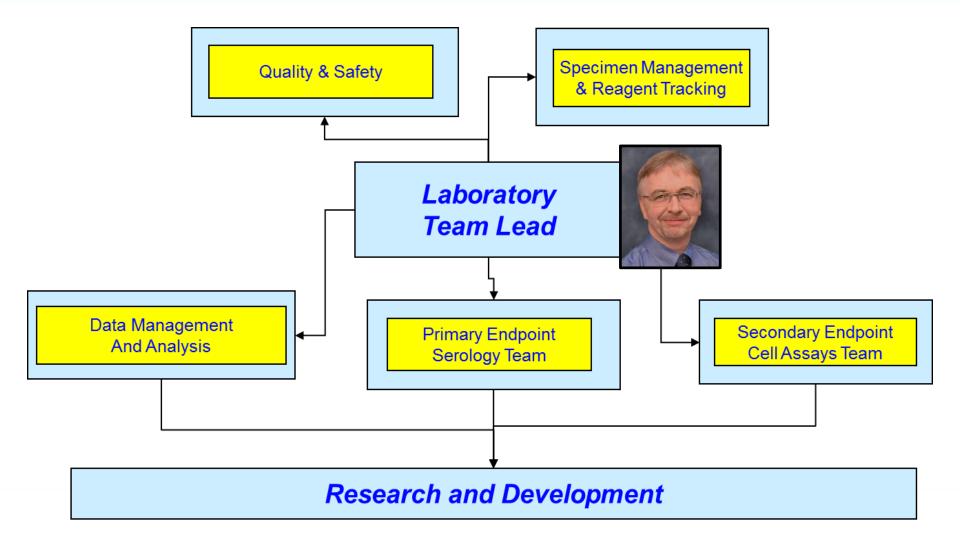


#### Quality and safety are integral and inseparable

- Regulatory compliant methods validation—ICH
- > QMS controlled and monitored processes and procedures

AVRP: Anthrax Vaccine Research Program QMS: Quality Management System CLIA: Clinical Laboratory Improvement Amendments ISO-9000: International Organization for Standardization-9000 CFR: Code of Federal Regulations ICH: International Conference on Harmonization

## Embracing a Culture of Laboratory Quality and Safety from Day 1



## An Effective QMS Encourages Public Trust in CDC Science and Recommendations

## Team development was guided by

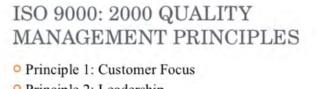
- Recognition that high public trust in CDC was an earned privilege
- Functional structure
- Specialized staff for specialized activities
  - Safety and quality management
  - Specimen management
  - Data management
  - Laboratory science

## QMS documented evidence

- Processes and procedures
- Competent and proficient
- Primary record data

# An Investment of Leadership and Management

- Ensure support from management
- Create the proper environment
- Craft a strategy
- Lead by example



- Principle 2: Leadership
- Principle 3: Involvement of people
- Principle 4: Process approach
- Principle 5: Systems approach for management
- Principle 6: Continual improvement
- Principle 7: Factual approach to decision making
- Principle 8: Mutually beneficial supplier relationships.
- "Perfection is not attainable, but if we chase perfection we can catch excellence" – Vince Lombardi

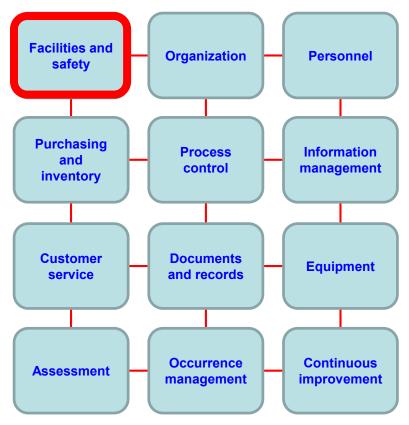


ISO: International Organization for Standards Verma U. www.slideshare.net/mtaram/total-quality-management-presentation-949360 linkedin.com/pulse/20141106190850-228512303-the-role-of-leadership-in-total-quality-management-tqm

## What Leaders Must Understand First

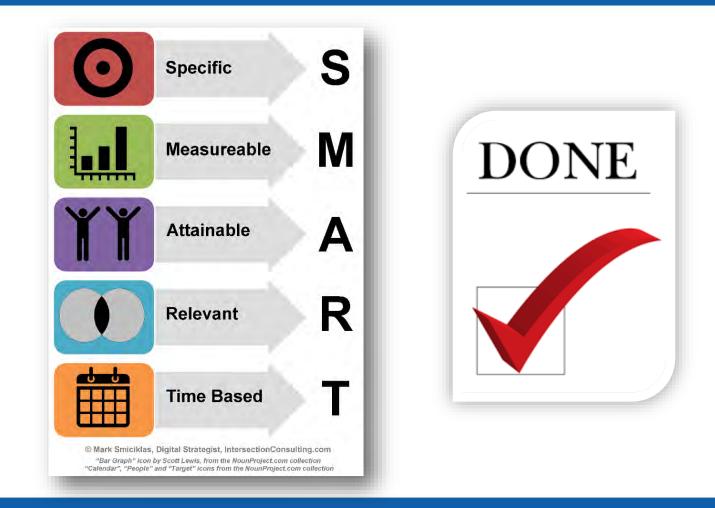
- What does the project I am leading involve?
- What are the benefits from success?
- Who benefits from success?
- What does my team need to succeed?

#### **The Quality Essentials**



Flaherty C. wwwn.cdc.gov/cliac/pdf/Addenda/cliac0208/Addendum%20T.pdf

## What Gets Measured, Gets Done



# Leaders Should Designate Resources Based on Initial Assessment

#### Make investments that are

- Tangible
- Sustainable

#### Develop assets including

- Personnel
  - Roles and responsibilities
  - Training
  - Skillsets
- Equipment
- Reagent standards
- Quality controls
- Standardized technologies
  - Data reduction and analysis



Soroka SD, Schiffer JM, Semenova VA, et al. *Biologicals*: 2010; 38(6): 675-683.

# **Resources Must be Valued and Protected**

### People are our most valuable resource

- Practice accountability and empowerment
- Know where you fit
- Own what you do
- Establish study-specific role descriptions
- Maintain training and competency records

## Protecting our state of the art facilities and equipment

- Perform preventative equipment maintenance
- Monitor performance
- Manage facilities and equipment





# Quality Management Systems (QMS): Building on Existing Expertise

#### Implementation of enterprise level LIMS

- Specimen and data management
- Study data management, analysis and reporting
- Specimen and critical reagent inventory
- Use existing agency expertise
  - Specimen barcoding
  - CASPIR inventory
  - Information management
  - Facilities management



# **Quality and Safety are Integrally Linked**

- Quality managers, safety liaisons, and team members should engage in
  - Developing risk assessments
  - Managing content
  - Controlling documents
  - Monitoring compliance
    - Requirements
    - Frequency
    - Competency



# **Laboratories Should Train With Intent**

### A core safety training curriculum is critical

Train like you fight, fight like you train

# What training do I need?

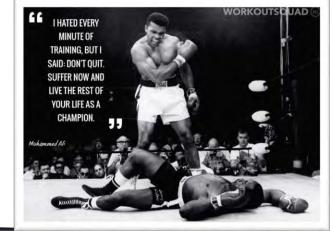
- Know where I fit
- Set clear expectations

# What am I trained to do?

- Defined curriculum
- Defined outcomes

# How do I know I am trained?

Competency based outcome and proficiency measures





medium.com/homeland-security/train-like-you-fight-and-fight-like-you-train-1787c0b78fde#.mctsiqn31 origami.about.com/od/History-Of-Origami/a/Akira-Yoshizawa-Origami-Biography.htm

# **Documenting Safety and the Quality of Science**

#### Document control system

# Laboratory risk assessments

- Process linked
- Biological and chemical hazards
- Risk mitigation and response

# Event and incident reporting

- Root cause analysis
- Impact assessment
- Corrective action
- Preventative action

	Laboratory:	Microbial Pathoge Response (MPIR)	(MPIR) Assessment (MPIR)		MPIR 6001-14	
	MP			SESSMENT FOR	10000	
1	TITLE	MPIR	6001-14 Working with Neisseria meningitidis Cultures			
1	Procedure		Manipulation of Netsseria meningitidis bacterial cultures.			
1	Team Lead	Li Han	Li Han Laborato			Bldg 18, B424
	Personnel	Applies	Applies to any MPIR Laboratory staff members using this procedure			his procedure
Title: Prepared Darts Bos	by: QA Review:		Approving Aur Name Consul Sugnature and I	hority: P. Quinn	( eng	Page L of 6
and a	National Center I	ni. 4 hazards for Disease Cout for Immunization Division of Bacter d Vaccine Preves	rol and Preventi and Respiratory tal Diseases (DB	ss (CDC) Diseases (NCIRD D)	9	
		Event Rep Attacl	ort #	-		
	tion of the Event					
Descrip	tion of the Event					
	use of Event:				1	4

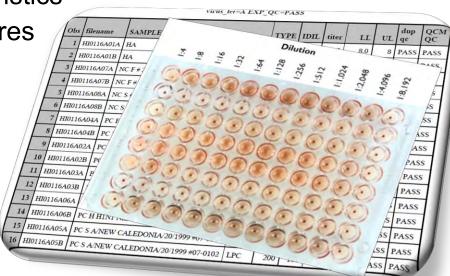
# Validated Science Adds Value and Confidence

#### Documented validation

- Defined performance characteristics
- Established acceptable measures of confidence and uncertainty

# Data management

- Traceable
- Transparent
- Reliable
- Secure reporting
- Evidence-based interpretation



# **Be Flexible**

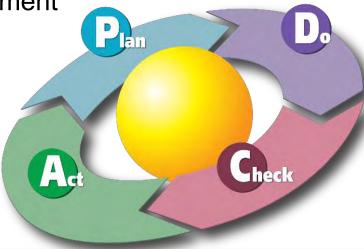
- "Effective leadership is putting first things first. Effective management is discipline, carrying it out"
  - Stephen Covey



# The Plan–Do–Check–Act Cycle

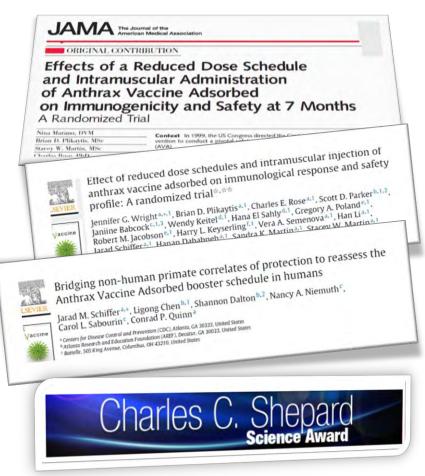
#### A process for implementing change

- > Plan: Recognize an opportunity and plan a change
- Do: Test the change start small
- Check: Review, analyze, and identify lessons learned
- Act: Take action based on lessons learned
- Repeat: Promotes continuous improvement
- Set targets quality indicators
- Measure progress
- Adapt to improve



## AVRP Demonstrates that Attention to Quality and Safety Does Not Compromise Productivity

- Laboratory tests for diagnosis and patient management
- Analysis models for immune correlates of protection
- A basis for regulatory action
- More than 70 laboratory specific publications
- More than 10 Patents
- Nine Shepard Award nominations



Marano N, Plikaytis BD, Martin SW, et al. *JAMA*. 2008;300(13):1532-1543. Wright JG, Plikaytis BD, Rose CE, et al. *Vaccine*. *2014*;*3*2(8): 1019-1028. Schiffer JM, Chen L, Dalton S, et al. *Vaccine*. 2015;33(31): 3709-3716. AVRP: Anthrax Vaccine Research Program

# **A Congressional Mandate Fulfilled**

#### A first for the anthrax vaccine

Only data-driven changes in AVA use in 38 years

#### Improved safety profile – 2008

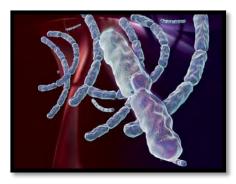
- Change to intramuscular injection route
- Reduction in frequency, severity and duration of injection site adverse events

#### Simplified regimen – 2012

- Reduction in priming series to 3 doses IM
- Protection in 6 months

#### Correlates of protection in humans

- > Application of the Animal Rule
- sBLA for booster schedule reduction 2016





# MPIR Laboratory Contributions to Enhancing Research and Collaboration

#### Emergency response capacity

- Anthrax letter attacks of 2001
- Pandemic H1N1 response contributions 2009
- STRIVE and Phase 1 Ebola vaccine studies
- Laboratory surge capacity

#### **Expertise**

- PEP anthrax vaccine optimization
- Pertussis and bacterial meningitis

#### Technology

- Methods development and technology transfer
- Emergency response laboratory capability

#### **Reputation**

- Associated funding
- Research-base expansion



Agrawal A, Lingappa J, Leppla SH. et al. *Nature*. 2003;424:329-334. Veguilla V, Hancock K, Schiffer J, et al. *Journal of Clinical Microbiology*. 2011;49(6):2210-2215. Fay MP, Follmann DA, Lynn F, et al. *Science translational medicine*. 2012;4(151):151ra126. MPIR: Microbial Pathogenesis and Immune Response STRIVE: Sierra Leone Trial to Introduce a Vaccine against Ebola PEP: post-exposure prophylaxis

# **Inspire Your Team**

- Recognize the value your team contributes to quality, safety, and public health or patient impact
- Share the vision you see for what the laboratory team can accomplish, and how it can best achieve its goals
- Articulate the importance of attention to safety and quality best practices
  - Catch people being good—recognize exemplary practices and performers
- **Continue to improve**

# **Embracing a Culture of Quality and Safety**

"Change will not come if we wait for some other person or some other time." — Barack Obama





"The illiterate of the 21st century will not be the person who cannot read. It will be those who cannot learn, unlearn and relearn." — Alvin Toffler

blogs.reuters.com/great-debate/files/2013/07/obama-best.jpg upload.wikimedia.org/wikipedia/commons/e/e1/Alvin\_Toffler\_02.jpg

# Establishing a Culture of Safety in an Academic Research Institution: Teaching Safety to Scientists



#### Joseph Kanabrocki, PhD, NRCM(SM)

Associate Vice-President of Research Safety Professor of Microbiology University of Chicago Chair, External Laboratory Safety Workgroup, CDC





U.S. Department of Health and Human Services Centers for Disease Control and Prevention

# **Building A Culture of Responsible Science**

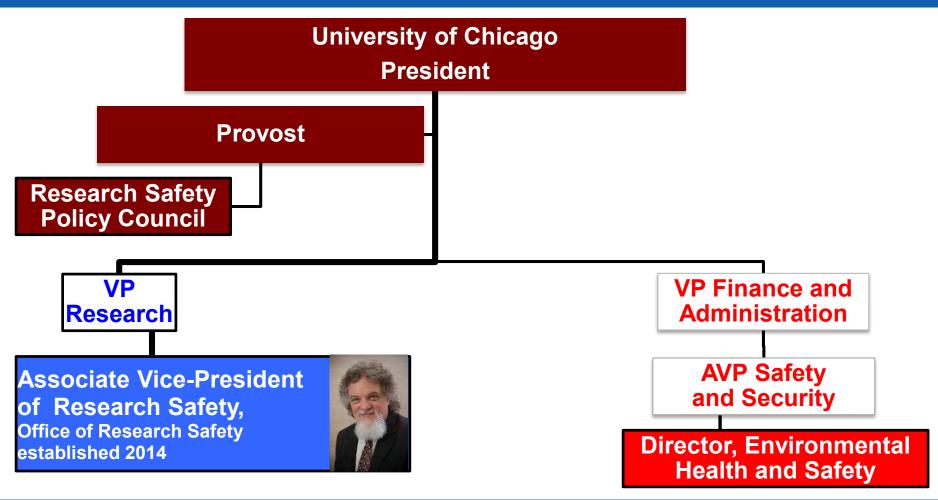
#### People

- > Provide leadership and support at all levels, especially high levels
- Develop and track training needs
- Support development of laboratory professionals

#### Institutional infrastructure and oversight

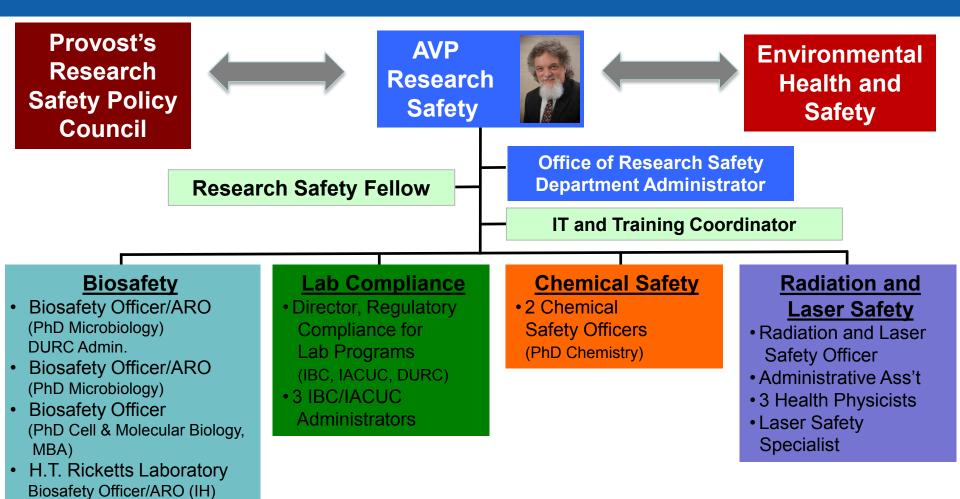
- Use institutional controls to assess and monitor risk
- Improve biosafety procedures
- Encourage reporting of incidents
- Knowledge, awareness, and communication
  - Engage broader community
  - Increase awareness through multiple media

# Leadership and Governance for Lab Safety at the University of Chicago



AVP: Associate Vice-President

# University of Chicago Office of Research Safety



AVP: Associate Vice-President IBC: Institutional Biosafety Committee IACUC: Institutional Animal Use and Care Committee DURC: Dual Use Research of Concern ARO: Alternate Responsible Official

# Risk Assessments: Institutional Biosafety Committee (IBC)

#### IBC is responsible for all life-sciences research protocols at University of Chicago

- Review and approval
- Surveillance

#### Review the use of biohazardous materials including

- Recombinant DNA
- Infectious agents
  - Humans
  - Animals
  - Plants
- Biological toxins

# Laboratory Safety Training

Laboratory safety training designed to meet needs of personnel working on research

Training requirements dictated by research description as detailed in IBC protocol

#### Variety of courses, matched to protocol needs

- Bloodborne Pathogens for Research Staff
- BSL1 and rDNA
- BSL2 and rDNA
- Viral Vectors
- Biological Toxins
- Human Gene Transfer (in development)
- Chemical Hygiene

# Cognitive and Practical Biosafety Education for the Host-Pathogen Investigator

- Intensive 4-day course
- Basic BSL3 lab safety, PPE, and respiratory protection
- Decontamination and disinfection
- History of biodefense programs, biologic toxins, biosecurity, and dual-use research
- Emergency response
- Epidemiology of lab-acquired infections
- Risk assessment of:
  - Recombinant DNA and pathogenic microorganisms
  - Laboratory animals and exposure
  - Vivarium and zoonoses

# Cognitive and Practical Biosafety Education for Host-Pathogen Investigators



Learning How to Prepare to Enter Laboratory Environment

# Cognitive and Practical Biosafety Education for Host-Pathogen Investigators



Learning how to put on personal protective equipment to enter BSL3 laboratory

**BSL: Biosafety Level** 

# Working with First Responders to Improve Understanding Risks in Laboratory Setting



First responders from the Argonne National Labs being shown laboratory work environment



## Responding to Ebola: Training Healthcare Workers How to Don and Doff PPE

- Ebola PPE protocol for healthcare workers similar to those used by laboratory workers
- Biosafety personnel rapidly developed training for proper use of PPE, clinical procedures, decontamination





PPE: Personal protective equipment PAPR: Powered air purifying respirators

# Shaping the Future: GLRCE Biosafety Research Fellow Program

#### One fellow per year in-residence program

NIH stipend, plus benefits

# Fellows support biosafety and IBC activities, with primary focus on laboratory and research safety

- IBC protocol review and risk assessment
- Select Agent Program management
- Laboratory inspections, including external inspections (USDA, CDC, FAA)
- Training
- BSL3 facility operations and maintenance
- Emergency spill response
- Export controls/DURC program and material transfer agreements

# Additional Experience for GLRCE Biosafety Research Fellows

- Fellows are expected to participate in applied biosafety research
- Fellows are encouraged to take advantage of resources and projects conducted at the H.T. Ricketts Laboratory (NIAID Regional Biocontainment Laboratory)
- Fellows attend and present at national and regional meetings
- Fellows prepare and sit for certification exams
  - National Registry of Certified Microbiologists (NRCM) and Specialist in Microbiology (SM)

GLRCE: Great Lakes Regional Center of Excellence for Biodefense and Emerging Infectious Diseases Research NIAID: National institute of Allergy and Infectious Diseases

# Using Applied Biosafety Research to Improve Safety and Facilitate Research

Two previously established University of Chicago autoclave standard operating procedures

Non-spore-formers: 40-min cycle at 121°C

Spore-formers (*B. anthracis*): 180-min cycle at 121°C

## Study found

- 40-min cycle safely decontaminates all infectious waste generated at H.T. Ricketts Laboratory (HTRL)
- Effective regardless of whether spores are in moist or dry waste
- Reproducible using several different types of bacteria

#### New SOP with reduced autoclave times

- Approved by IBC
- Increased efficiency and safety of operations

SOP: Standard Operating Procedure IBC: Institutional Biosafety Committee Helm RA. Unpublished data, reviewed by University of Chicago Institutional Biosafety Committee.

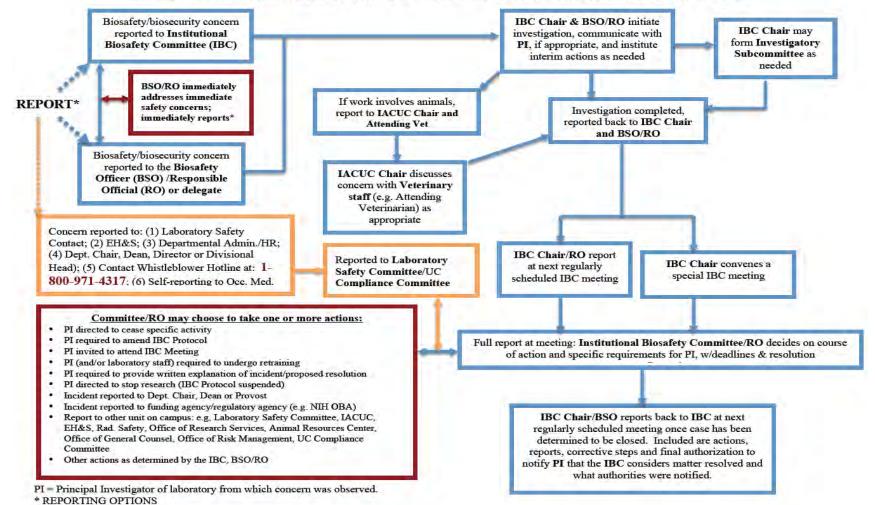
# GLRCE Programmatic Legacy and Direct Impact: Biosafety Fellows

# Previous fellows now work in key laboratory safety positions with various organizations including

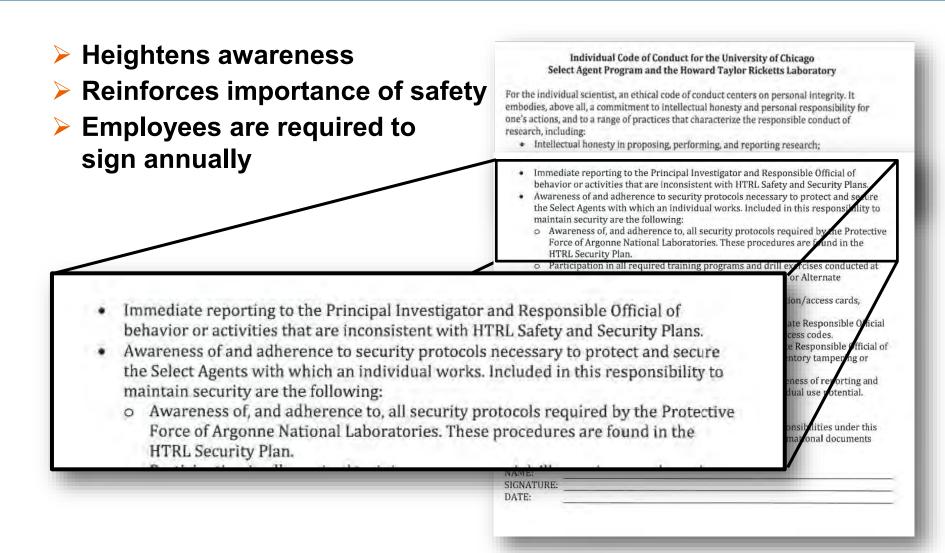
- Universities
  - Massachusetts Institute of Technology
  - Northwestern University
  - University of Chicago-Hyde Park
  - University of Cincinnati
  - University of Illinois at Chicago
  - University of Nebraska-Lincoln
  - Washington University in St Louis
- Research Institutes
- Governmental Agencies (DHS)

# Incident Reporting Is Encouraged: Multiple Reporting Pathways Established

#### **IBC PROCEDURES FOR DEALING WITH BIOSAFETY/BIOSECURITY CONCERNS**



# **Code of Conduct Includes Reporting Incidents**



Services Provided by University of Chicago Office of Research Safety

## "How do we get investigators to even know we exist?"

"How do we get investigators to realize we are here to help?"

# Communication and Outreach to Frontline Laboratory Workers





#### **DO NOT APPLY COSMETICS IN THE LAB** (THIS INCLUDES CHAPSTICK®)

## DON'T EAT OR DRINK OR STORE FOOD IN THE LAB. DON'T HANDLE CONTACT LENSES IN THE LAB.



http://biologicalsafety.uchicago.edu/

This message brought to you by the Office of Biological Safety and BSL Awesome Productions.



# YOU SHALL NOT PASS



# ...IBC approval without the appropriate biosafety training.

biologicalsafety.uchicago.edu/ facebook.com/UChicagoBiosafety This message brought to you by the Office of Biological Safety and BSL Awesome Productions.







THE NIH GUIDELINES, OR THE NIH GUIDELINES FOR RESEARCH INVOLVING RECOMBINANT AND SYNTHETIC DNA MOLECULES, IF YOU'RE NOT INTO THE WHOLE BREVITY THING, APPLY TO ALL RESEARCH INVOLVING rDNA AND SYNTHETIC DNA REGARDLESS OF ITS FUNDING SOURCE.

FOR ANY QUESTIONS REGARDING COMPLIANCE WITH THE NIH GUIDELINES, CONTACT THE OFFICE OF BIOLOGICAL SAFETY

773.834.2707 biosafety@ bsd.uchicago.edu



# **Clever Posters Designed to Increase Awareness**

#### Introducing The Most Interesting Man in Biosafety.



This message brought to you by the Office of Biological Safety and BSL Awesome Productions. http://biologicalsafety.uchicago.edu/



## ... and Reinforce Good Behavior

#### I don't always work with recombinant or synthetic DNA...



#### But when I do, I have an IBCapproved protocol.

This message brought to you by the Office of Biological Safety and BSL Awesome Productions. http://biologicalsafety.uchicago.edu/



# How to Strengthen A Culture of Lab Safety

#### Leadership at high levels

- UC Office of Research Safety
- CDC Office of the Associate Director for Laboratory Science and Safety

#### Developing future leaders

- UC GLRCE Biosafety Research Fellows
- CDC Laboratory Leadership Service

#### Review mechanisms for lab safety

- UC Institutional Biosafety Committee
- CDC Laboratory Safety Review Board

#### Engaging and proactive communication

# **Questions?**

Selected CDC Pathogen and Toxin Discoveries



Akhmeta Virus



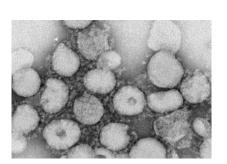
Legionella



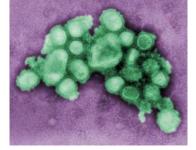
Bourbon Virus



Lychee Nut Toxin



SARS





2009 pandemic H1N1 Influenza

Carcinogens in Smoke

For more information about CDC Laboratory Safety www.cdc.gov/about/lab-safety/index.html

PHIL ID 14542, 11215, 15530, 11152, 19479