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

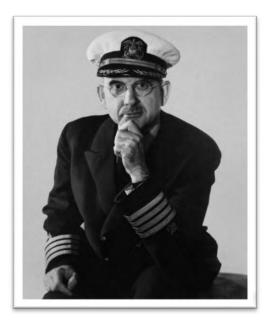
Associate Director for Laboratory Science and Safety Centers for Disease Control and Prevention



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:

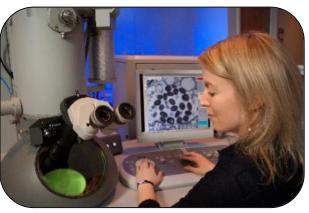
- Infectious diseases
- Noninfectious diseases
- Environmental health
- Occupational health
- Laboratory systems (e.g. standards, quality guidelines)



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



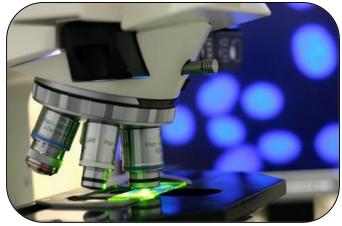
Laboratory Staff

- 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

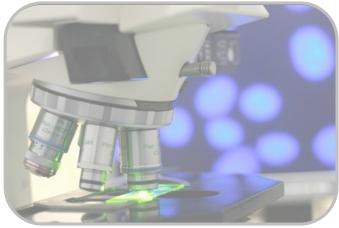
□ BSL-4:

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

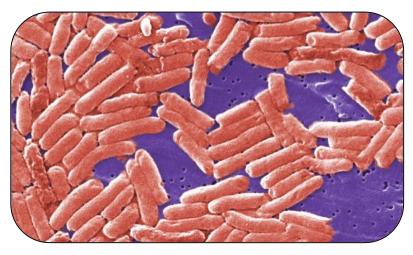
Over 2,000 laboratory staff



Over 150 laboratory groups



Over 200 infectious pathogens



Pathogens

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

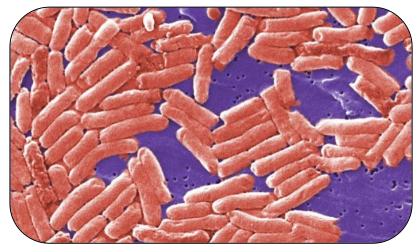
Over 2,000 laboratory staff



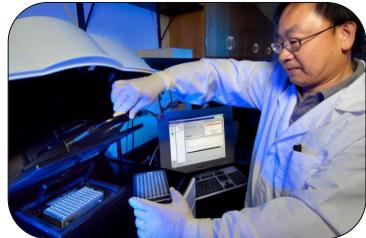
Over 150 laboratory groups



Over 200 infectious pathogens



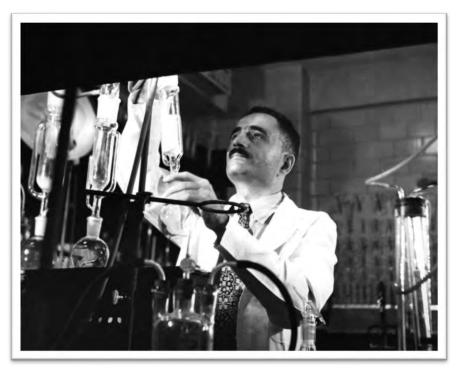
Over 5,000 samples processed per day



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



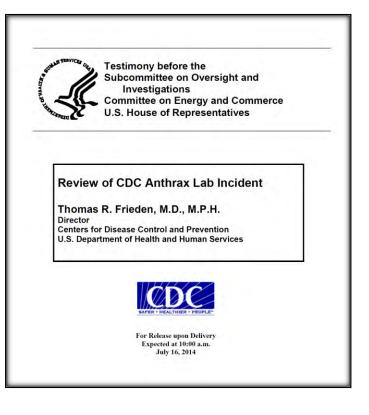
A scientist works with infectious influenza virus without modern personal protective equipment (PPE)

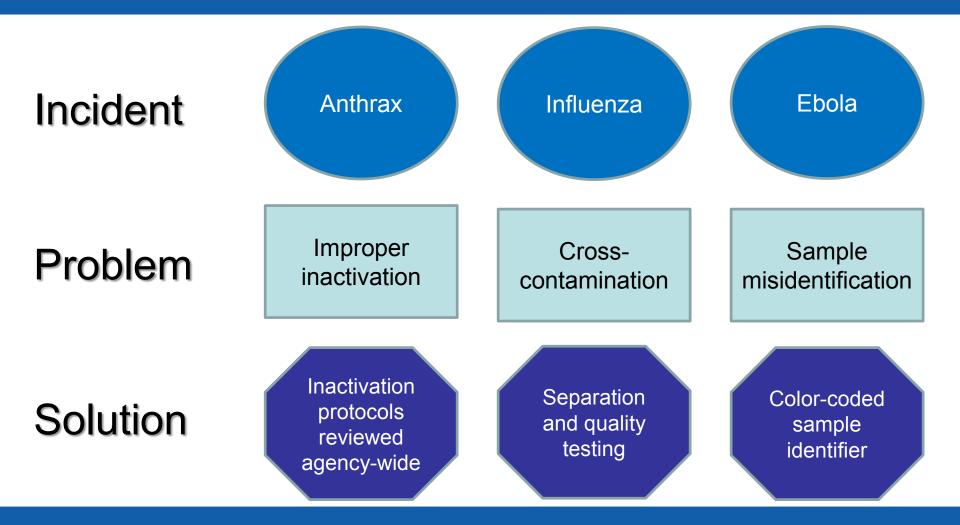


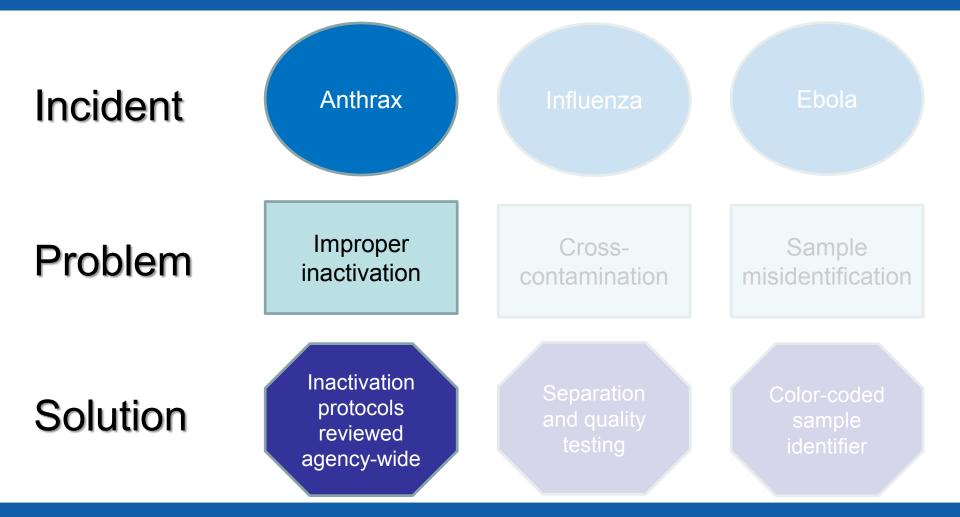
Today, scientists use biological safety cabinets (BSC) and powered air purifying respirators (PAPR) when working with highly pathogenic avian influenza virus

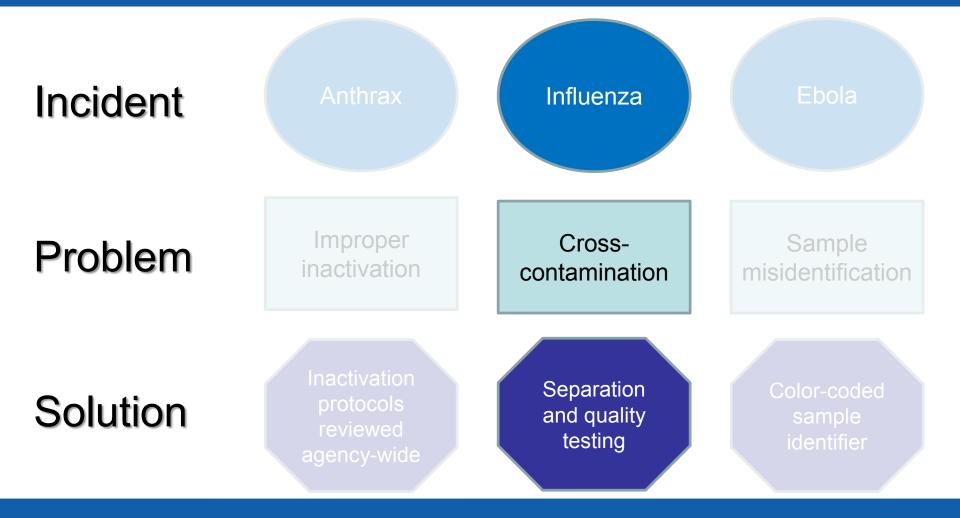
"What we're seeing is a pattern that we missed, and the pattern is an insufficient culture of safety."

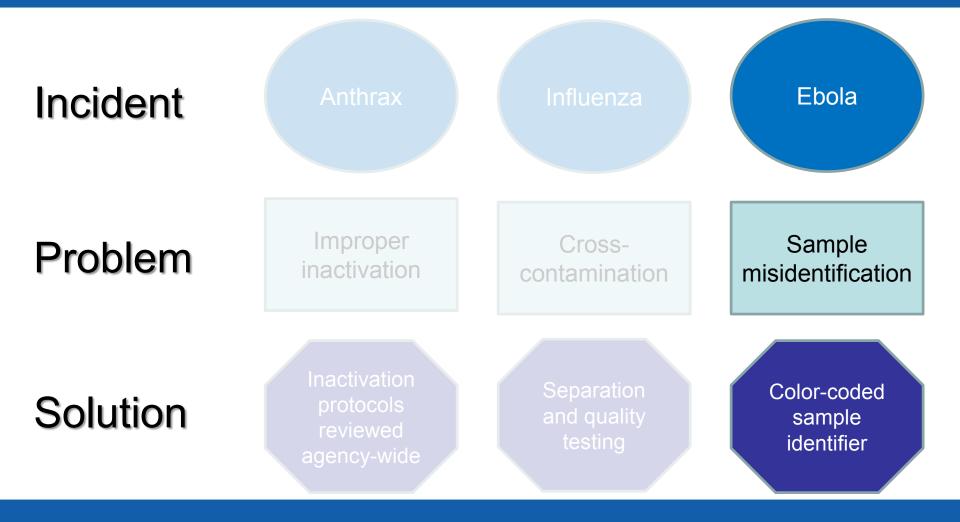
> Dr. Thomas Frieden, Director, CDC











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

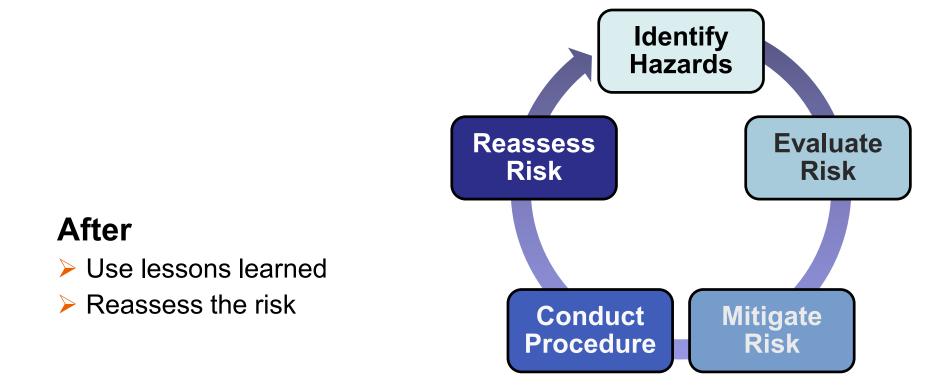
- Ensure research benefits outweigh the risks
- Explore safer alternatives
 - Use of non-pathogenic strains
- Predict potential problems



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

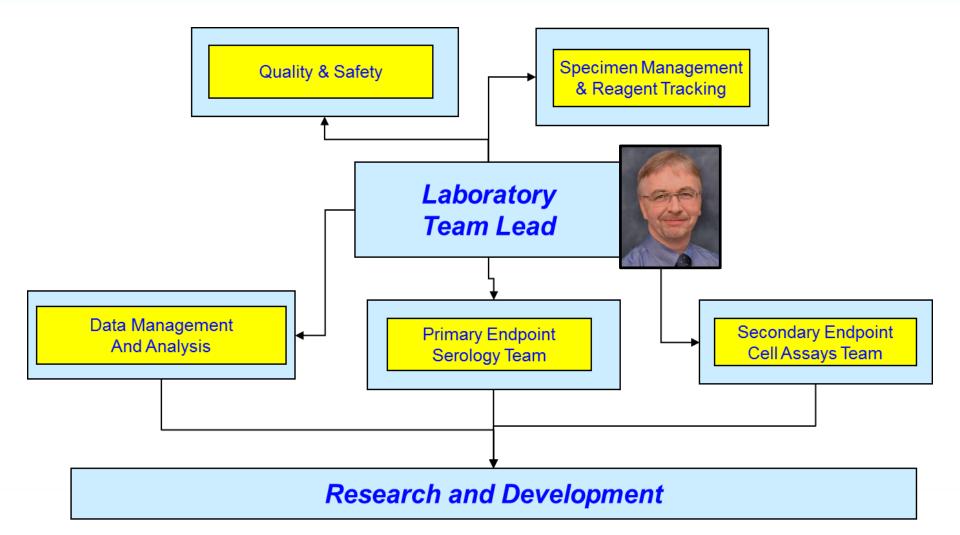


Quality and safety are integral and inseparable

- 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

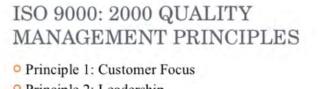
- Recognition that high public trust in CDC was an earned privilege
- Functional structure
- Specialized staff for specialized activities
 - Safety and quality management
 - Specimen management
 - Data management
 - Laboratory science

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

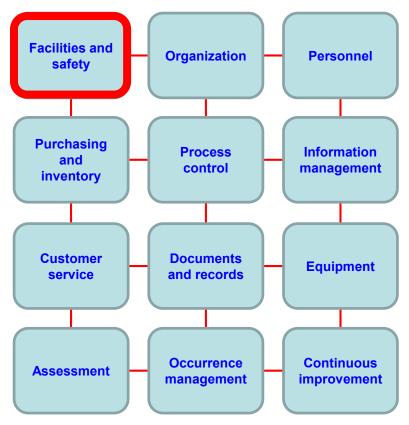


ISO: International Organization for Standards Verma U. www.slideshare.net/mtaram/total-quality-management-presentation-949360 linkedin.com/pulse/20141106190850-228512303-the-role-of-leadership-in-total-quality-management-tqm

What Leaders Must Understand First

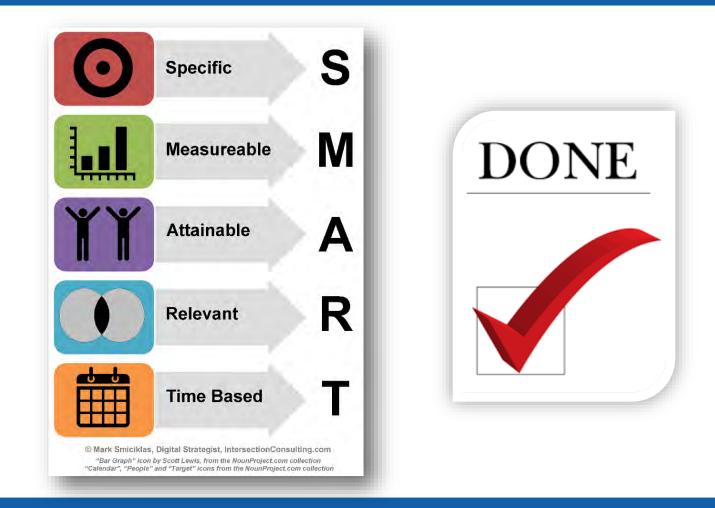
- What does the project I am leading involve?
- What are the benefits from success?
- Who benefits from success?
- What does my team need to succeed?

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

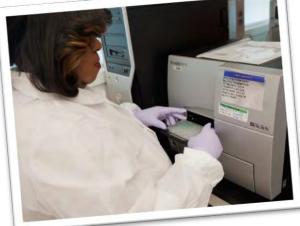
People are our most valuable resource

- 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?

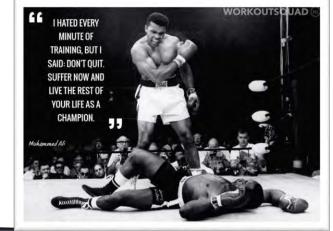
- Know where I fit
- Set clear expectations

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
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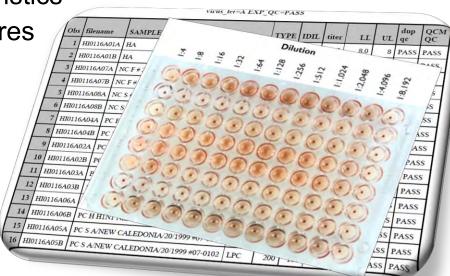
Validated Science Adds Value and Confidence

Documented validation

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

Data management

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



Be Flexible

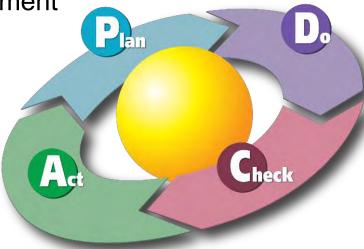
- "Effective leadership is putting first things first. Effective management is discipline, carrying it out"
 - Stephen Covey



The Plan–Do–Check–Act Cycle

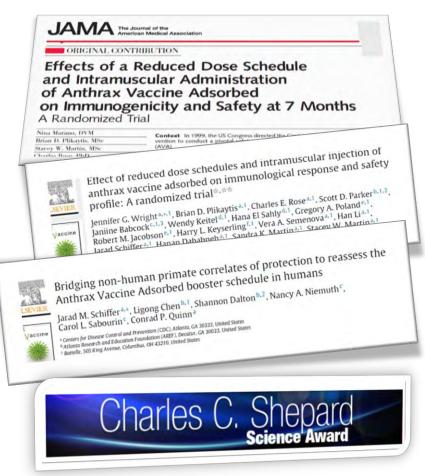
A process for implementing change

- > 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

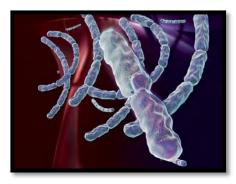
- Change to intramuscular injection route
- Reduction in frequency, severity and duration of injection site adverse events

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

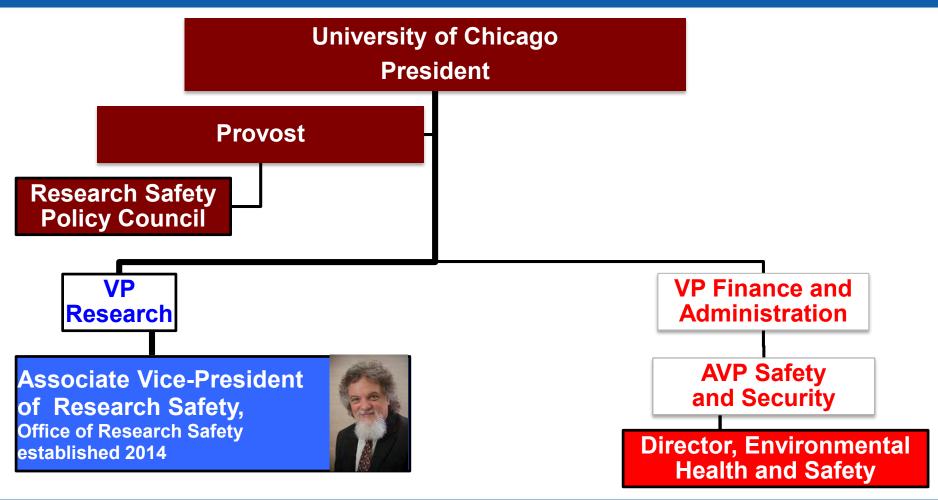
People

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

Institutional infrastructure and oversight

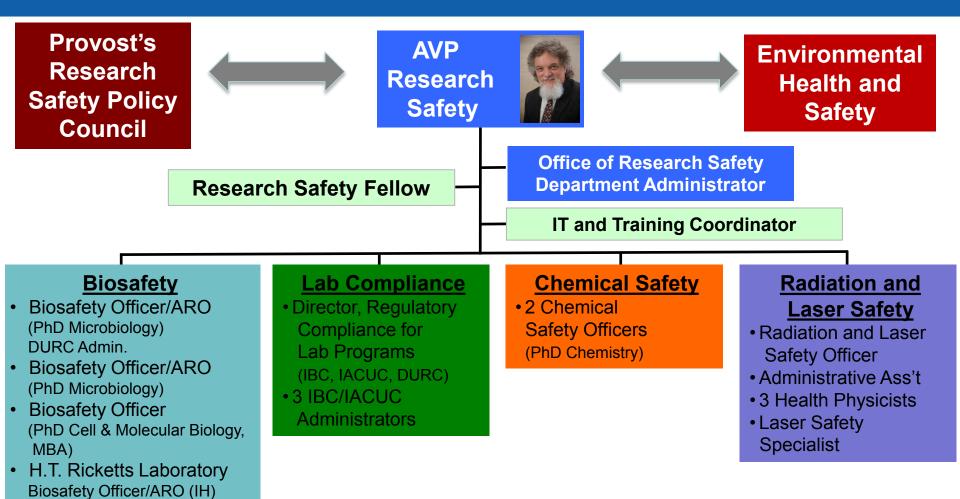
- Use institutional controls to assess and monitor risk
- Improve biosafety procedures
- Encourage reporting of incidents
- Knowledge, awareness, and communication
 - Engage broader community
 - Increase awareness through multiple media

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.

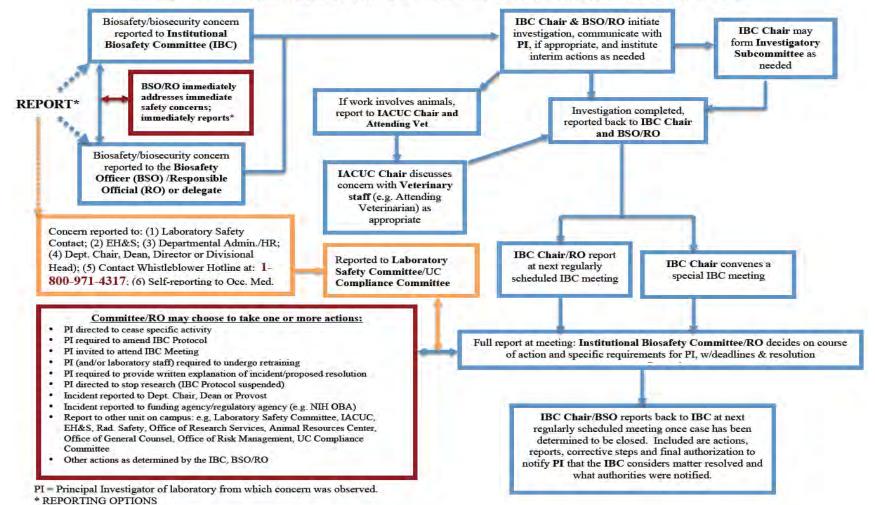
GLRCE Programmatic Legacy and Direct Impact: Biosafety Fellows

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

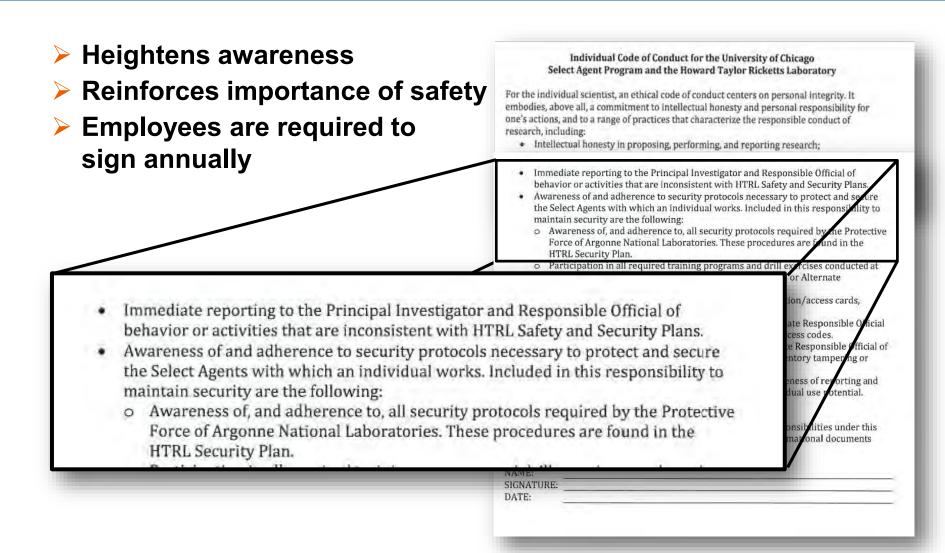
- Universities
 - Massachusetts Institute of Technology
 - Northwestern University
 - University of Chicago-Hyde Park
 - University of Cincinnati
 - University of Illinois at Chicago
 - University of Nebraska-Lincoln
 - Washington University in St Louis
- Research Institutes
- Governmental Agencies (DHS)

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.

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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

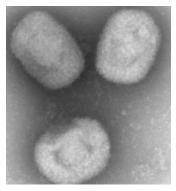
Review mechanisms for lab safety

- UC Institutional Biosafety Committee
- CDC Laboratory Safety Review Board

Engaging and proactive communication

Questions?

Selected CDC Pathogen and Toxin Discoveries



Akhmeta Virus



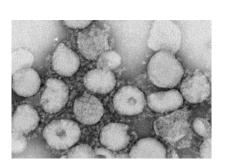
Legionella



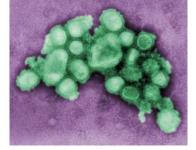
Bourbon Virus



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

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