April 2012 Meningococcal Fatality
October 6, 2014 ABSA Conference

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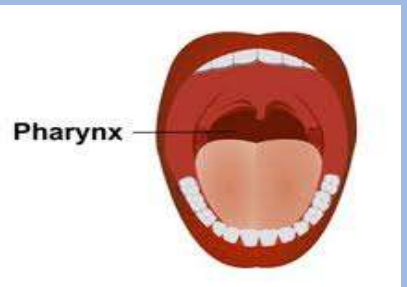
Disclaimer

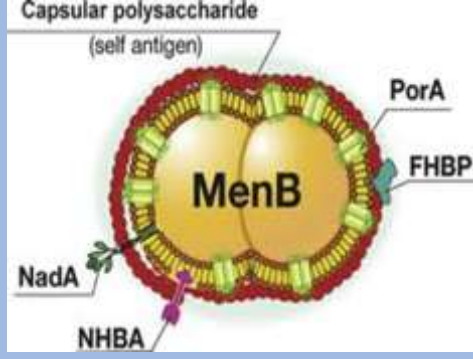
I acted as an independent biosafety consultant during this investigation. The opinions expressed during this lecture do not represent the opinions of the California Department of Public Health.

About the organism
Neisseria meningitidis

- Gram-negative diplococci
- Humans are the only natural reservoir
- Attaches to surface of mucosal cells of nasopharynx
- Up to 10% of persons are colonized
- Transmitted from human to human by direct contact with respiratory secretions (i.e. coughing & sneezing)



Neisseria meningitidis



- Produces a polysaccharide capsule which is basis of serogrouping, molecular identification, and vaccine
- 13 serogroups have been identified
- Majority of disease worldwide is: A, B, C, Y, and W
- Serogroups B, C and Y are most common in the U.S.
- Serogroup B is responsible for approximately 30-40 % of cases in California
- No FDA approved vaccine for serogroup B in most countries (there are serogroup B vaccines in New Zealand, Cuba, and Europe)

Meningococcal Disease

- Leading cause of bacterial meningitis:

  CA: 150-200 cases per year

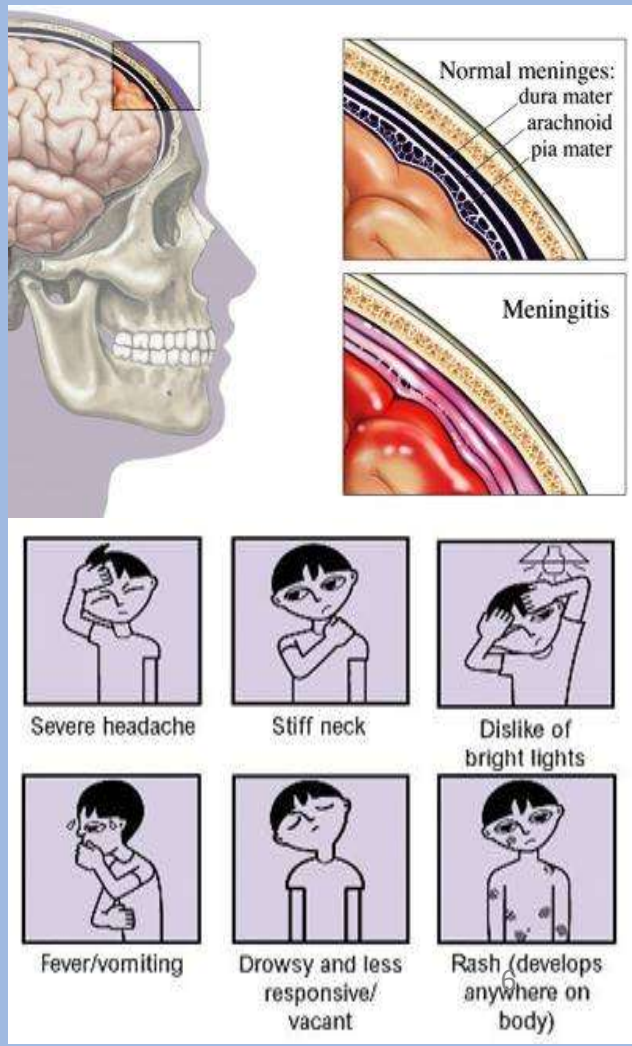
  US: 1,400 – 2,800 cases per year

  800-1, 200 cases per year (2005-2011)
- Reportable
- Incubation period 1-10 days (usually <4 days)

- Causes substantial morbidity: 11-19% survivors have sequelae (neurologic disability, limb loss, hearing loss)

Clinical Presentation

- Septicemia – most severe
- Many deaths within 12 hours/almost all within 48 hours
- Meningitis
- Coma
- Pneumonia
- Pyogenic arthritis
- Pericarditis
- Conjunctivitis



Meningococcal Immunizations

- **MCV4 Quadrivalent conjugate vaccine**, contains capsular polysaccharide antigens (A, C, Y and W-135)
- High risk persons 2-55 years (e.g., persons with complement deficiencies or asplenia, laboratory workers, travelers)
- *New ACIP Guidelines Published March 2013*allows use in persons over 55

- **MPSV4** is a **tetravalent meningococcal polysaccharide vaccine** (A, C, Y, W-135)
- Recommended for persons 55 and up
- Booster dose recommended at 5 year intervals


MENINGOCOCCAL VACCINE

WHAT YOU NEED TO KNOW

Case History

Case History Friday April 27

- Graduated from a local university with a degree in Microbiology in August of 2011.
- Began working in a San Francisco Veterans Administration Medical Center (SFVAMC) research lab in October 2011.

- Worked with serogroup B & Y isolates the week of his death
- He was out ill 4.5 days during the month of April

- Last work day on Friday 4/27

- By early evening he wasn't feeling well

Case History April 28, 2012 ER

- Left for hospital at 10:30 am
- Roommates drove him to the ER- he lost consciousness in the car.
- 25 year old male, previously healthy, presented with complaint of fever, headache, chills, vomiting for one day.
- Patient coded, and was intubated.
- Obtunded with a diffuse petechial rash.
- Head ER physician instructed all health care workers to don an N95 respirator.

Saturday, April 28, 2012 in the ER

- One blood culture was drawn.

- The patient received one dose of ceftriaxone and vancomycin
- Lumbar puncture was not performed

- Other labs consistent with profound sepsis (e.g. acidosis, pancytopenia).

- Resuscitation continued- He was declared after 3 hours of heroic efforts.

Saturday, April 28, 2012

- Because of concern for meningococcemia, the on-call ID attending was notified.
- Approximately 25 ER staff were identified as having been in close contact (e.g. in the same room) with the patient during his prolonged resuscitation.
- All were given Ciprofloxacin 500 mg x 1; one pregnant staff received ceftriaxone 250 mg x 1 IM.
- Roommates and friends with close contact in the last 48 hours were contacted and also given Ciprofloxacin 500 mg x 1
- SFDPH and CDPH were notified.

Saturday, April 28, 2012, evening

- PI of the lab was out of town.
- Lab voluntarily closed down and decontaminated with bleach.
- Lab staff were contacted and informed of potential exposure.
- No staff reported symptoms reported
- Staff were advised to go to the ER to receive ciprofloxacin

Monday, April 30, 2012

- Hospital held a town hall to educate staff about meningococcal disease.
- 60 doses of ciprofloxacin were administered in the next 24 hours.
- At 48 hours, the single blood culture had not grown any organism.
- Unable to isolate *N. meningitid*is from tissue
- PCR of the blood performed by CDPH Microbial Diseases Laboratory (MDL) was positive for meningococcus serogroup B.
- Blood and tissues samples forwarded to CDC for strain typing

Laboratory Inspection

California Aerosol Transmissible Disease Standard CCR Title 8 Section 5199 (f)

- Identification of Biosafety Officer
- Risk Assessment in accordance with BMBL
- Implement feasible work practice controls in accordance with the BMBL
- Develop a list of job classification, tasks, and procedures where employee exposures might occur
- List of ATP-L that are present in the lab
- Safe handling procedures
- Engineering Controls (biosafety cabinets, transport carriers)
- PPE
- Decontamination of surfaces and equipment
- All incoming materials containing ATPs-L be treated as containing the virulent pathogen
- Inspect labs and biosafety procedures annually
- Emergency procedures for uncontrolled releases
- Procedures for medical services including (e.g. IZ, Tx)
- Procedure for review of biosafety plan

ATD-L Appendix D
Mandatory for Laboratories

"*Neisseria meningitidis* (activities with high potential for droplet or aerosol production, large quantities or high concentrations)"

January 5, 2012 MMWR Supplement to BMBL

"Precautions beyond the standard and special practices for BSL-2 may be indicated in the following circumstances:

- Suspected high-risk organism (e.g. *Neisseria meningitidis*)
- Work with large volumes or highly concentrated cultures
- Compromised immune status of staff
- Training of new or inexperienced staff"

- Prescription eye glasses are not to be considered eye protection

BMBL 5th Edition published 2009 recommends BSL-2 containment practices for *N. meningitidis* work

BSL-2 Enhanced or BSL-2+

- BSL-2 laboratory
- All infectious work takes place in BSC
- Some BSL-3 practices are implemented
- BSL-3 PPE is used including
  - closed front disposable lab coat
  - double gloves
  - eye protection
  - N95 or higher respirator

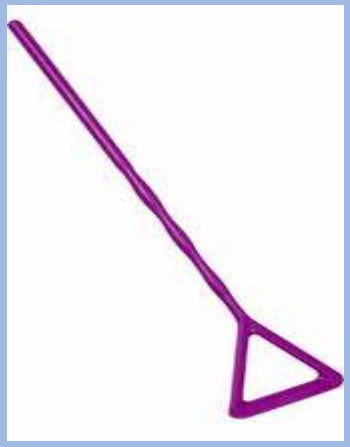
Source Specimens

- 1ml stock culture
- Inoculated selective GC media plates

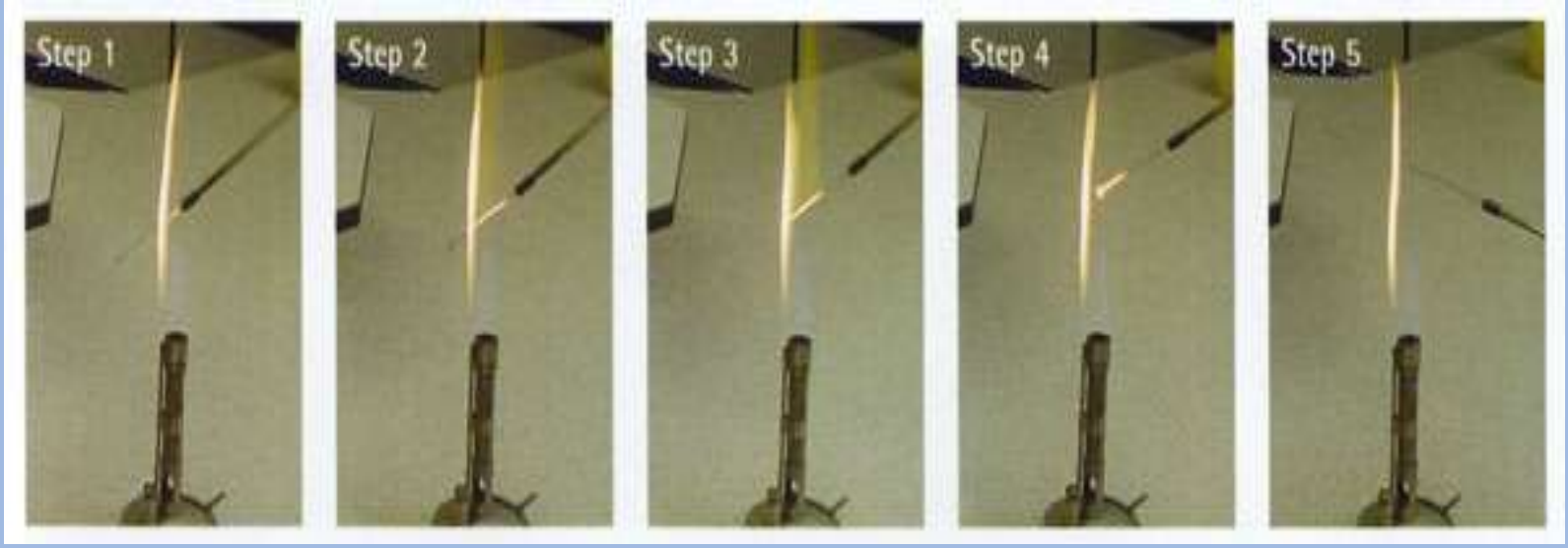
Transporting specimens

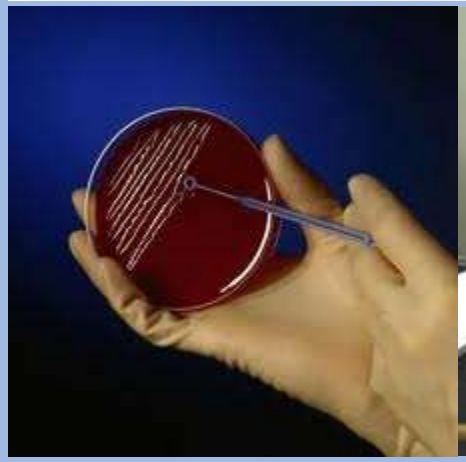
Transported isolates within the room by hand

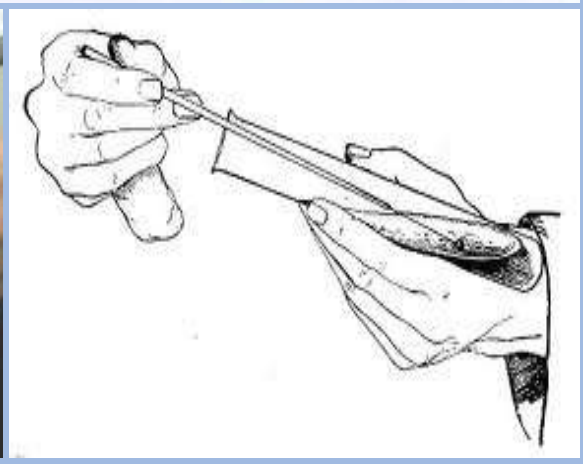
Equipment



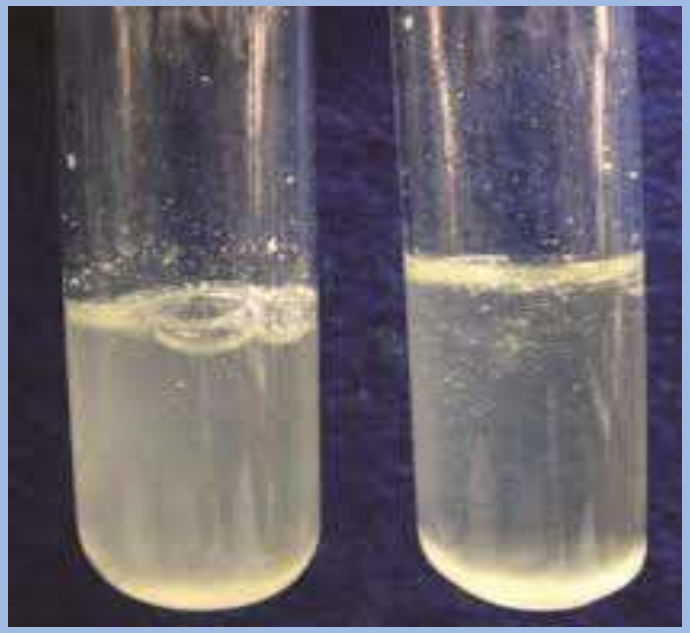
Inoculation of the plate & subculture







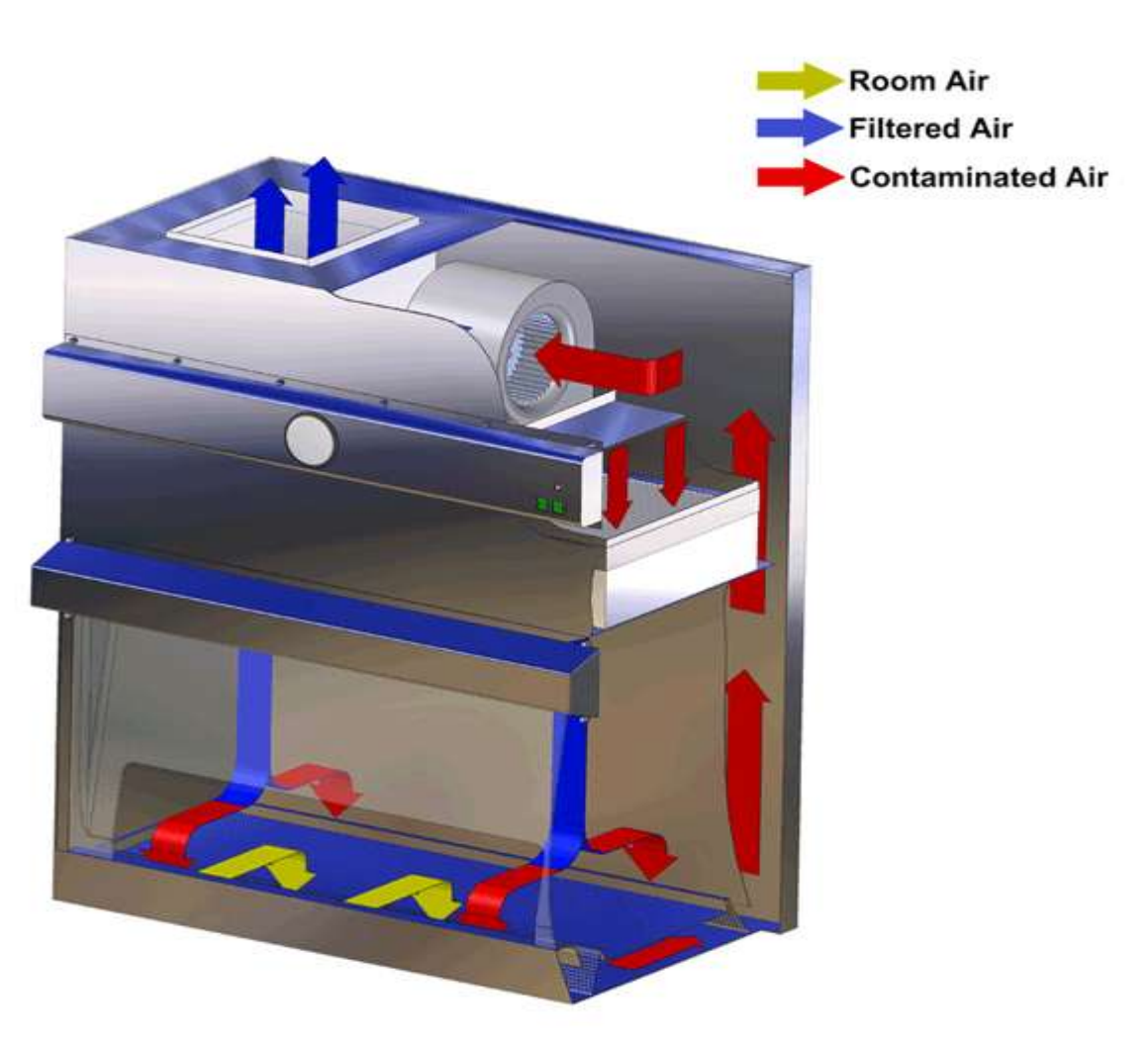
Lysozyme Enzymatic Reaction



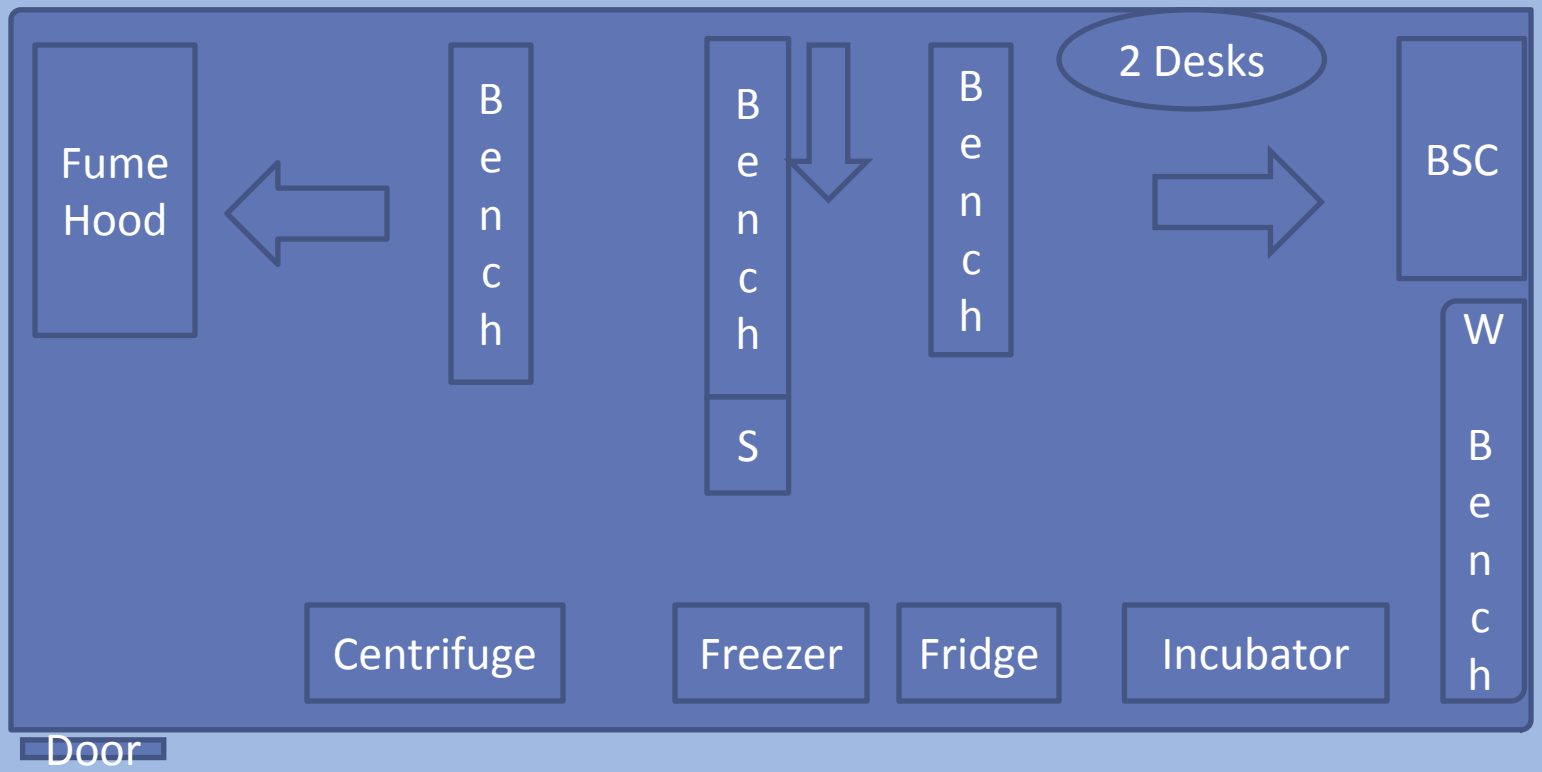
Biohazard waste

- Biohazard bin
- Biohazard waste removed by VA EMS, chemicals by VA CHMT
- Requested a visit to the medical waste area

BSC Airflows



Laboratory Layout



Inspection Findings

- Didn’t always wash hands
- Worked outside of BSC
- Decontaminated work surfaces with 70% ethanol
- Flaming of transfer loop
- Heat fixing of damp gram stain slide
- Plate spreading
- Plate scraping
- Disposal of scrapers and spreaders
- Disposal of plates
- Lysozyme inactivation step not validated or verified
- Vigorous pipetting of lysozyme

Improvement Plan

Target Procedures
- Gram stain
- Culture transport
- Culture inoculation
- Pipetting lysozyme
- Plate harvesting

Decontamination
- Disinfectant/Contact time
- Enzymatic reactions
- Wipe down carriers before removing from the BSC
- Wipe down biohazard bag before removing from the BSC

Procedures
- Post spill procedure near work area
- Review workstation setup procedure

Engineering Controls
- Verify BSC airflows
- Pull sash to marked level

Inventory
- Keep current records (inventory/notebook)
- Identify cultures working with daily

PPE
- Eye Protection
- Double Gloves
- Disposable lab coats or launder

Medical Surveillance
- Vaccination
- Post-exposure plan

Training
- Train staff in ATDs
- Signs & symptoms
- Review laboratory techniques

Supervision
- Limit weekend work
- Mentor junior microbiologists
- Assess competency

Federal OSHA Issued Citations

- **29 CFR 1960.8(a):** The Agency head did not furnish a place of employment to each employee that was free from recognized hazards that caused or were likely to cause death or serious physical harm in that the U.S. Veterans Administration failed to offer available **vaccines** for strains of *Neisseria meningitidis* to which employees were exposed

- **29 CFR 1960.8(d):** The Agency did not require employee(s) to use approved **safety equipment**

- **29 CFR 1960.59(a):** The Agency did not provide **specialized job safety and health training** appropriate to the work performed by the employee.

Status Case Closed

The VA had 15 days from the issue of the citations to respond. The VA attorneys decided to appeal. The family filed suits against the VA & university. Three defendants were implicated in the suit. The court threw out the charges against the defendants, but the allowed them to pursue the United States of America. The plaintiff decided not to sue the USA. Case was dismissed March 18, 2014.

References

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