Miller, Diane M.

From: William James |
Sent: Tuesday, March 22, 2005 3:50 PM
To: NIOSH Docket Office
Cc: Robert Lawson; PIT-NPPTL-Internet-Input; John Danby
Subject: Fw: Mark Nicas on Respiratory Protection for Bioaerosols

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Niosh Docket Office:

I received the message below from an industrial hygienist at the Lawrence Livermore Laboratory, with the presentation by Mark Nicas on respiratory protection for bioaerosols. The statement on the top of the first page of the presentation directs comments on the material to you. I took the time to read this somewhat thoroughly because I am responsible for implementing the respiratory protection program at the UC Davis Medical Center. I have decided to send you my comments because I realize that the final recommendation in this presentation could have major impact on how most health care facilities run their respiratory protection program. Here are my comments for consideration:

1. A protection factor of 1000 (0.1% leakage) is assumed for a hooded PAPR to compare to a protection factor of 10 for an N95 filtering facepiece, which eventually leads to a calculated risk difference of a factor of 100 for protection from exposure to bioaerosols and the recommendation to use PAPRs instead of N95 masks. Currently, I believe there is a lot of disagreement on what should be the assumed protection factor for hooded PAPRs (as well as other types of PAPRs). Some sources say that the protection factor should be assumed to be as low as 50. In fact, the NIOSH "Interim Recommendations for the Selection and Use of Protective Clothing and Respirators Against Biological Agents" (October 2001) indicates that a PAPR with a HEPA filter provides a protection factor of 50. From observing quantitative fit test results for tight fitting respirators, I know that a PAPR with HEPA filters (P100) has a much higher protection factor than an N95 filtering facepiece, but NIOSH should include the rationale for using a higher protection factor for the PAPR in these calculations than those recommended by other respected sources if this presentation is adopted.

2. The calculations that eventually produce the risk levels in the first example of exposure to small pox bacteria (3% for N95 use, 0.03% for hooded
PAPR) discussed in the presentation do not include the consideration of air cleaning (air changes per hour) in the room that a health care worker would be exposed. Typical isolation rooms should have 12 air changes per hour or more which cleans the air rapidly, so this example should state that the air concentration level assumed and risk level calculated are from a simplistic scenario that does not account for the dynamics of ventilation in the area of exposure. The risks calculated appear to have been produced just to show that a PAPR filters out 100 times more particles, and hopefully not to convey actual risks that workers can be expected to be exposed to. To get closer to real risks, we need to better estimate the real air concentrations they could be exposed to.

3. The second example set of calculations for risk from M. tuberculosis do a good job of estimating the average generation rate of respirable bacilli coughed into the air per hour, but the discussion that follows this leading to an estimated risk of 9.5% for N95 protection and 0.1% for PAPR protection does not seem connected well with the earlier calculations - to the point that the risks look somewhat pulled out of the air. In trying to make sense of this, assume that the calculated generation rate of 1.5 respirable bacilli per hour is coughed into a 50 cubic meter room, then the risk to a worker of inhaling a bacilli in one hour of work is:

1 m3 breathed x 1.5 bacilli / 50 m3 = 0.03 or 3% (assuming 1 m3 breathed per hour and the bacilli has equal probability to be anywhere in the room air and no probability to deposit on a surface in the room)

Then take into account ventilation cleaning affect of room air changes, and this probability would be much lower. Then take into account the protection factor of the N95 or PAPR. So, I think when accounting for a realistic scenario of a patient coughing out 1.5 respirable bacilli/hr into a typical isolation room (12 air changes per hour) and the worker wearing an N95 respirator for one hour of work in the room, then the probability of the

worker inhaling that bacteria could be well below 1%.

In summary, the effort of the presenter is appreciated in that an overall quantitative approach in estimating a worker's risk to bioaerosols is developed and it certainly can be useful in determining acceptable respiratory protection. It is just good to make a point of the important variables in real situations that should be considered to refine these risk estimates, especially if the risk estimates are going to be used by policy makers. Further work on this should be done before ruling out the usefulness of the N95 respirator in many health care situations. Can there be a "graded approach" - should PAPRs be required for high risk health care situations and the N95 respirator allowed for lower risk situations?

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Respirator Selection for Airborne Infectious Agents

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Some Pathogens Transmitted Person-to-Person via Air

Mycobacterium tuberculosis

SARS virus

Variola virus (smallpox)

Yersinia pestis (pneumonic plague)

Intertwined Views

- Infection is often due to droplet transmission (spraying of non-inspirable particles onto mucous membranes).
- Close contact is required for infection, because droplets do not travel far.
- Close contact is required even if exposure is via inhalation, because infection risk is inherently low.

Given These Views …

An N95 filtering-facepiece respirator is judged to be sufficient:

- **as a barrier to prevent droplet contact**
- **as a means to prevent inhalation exposure**

However ...

- Where droplet transmission can occur, so can inhalation transmission. Droplets up to 100 μm can be inspired, although close contact is required.

- Some pathogens have an infectious dose as low as one organism (*M. tuberculosis*, variola virus) and can be carried on respirable particles. In this case, close contact is not required for infection.

- If one organism can infect, a low pathogen concentration in air can impart a high risk of infection.
- N95 masks permit 10% inward leakage of contaminated air around the faceseal.
- The residual risk with use of an N95 respirator may still be substantial.

Example - Smallpox

- The infectious dose appears to be a single virus (Nicas, Hubbard, Jones and Reingold, *Applied Biosafety 9*:118-127, 2004).
- Airborne infection is via droplet transmission and inhalation.
- It has been recommended that HCWs attending smallpox patients (related to bioterrorism) use N95 masks.

When One Microbe Can Infect

- Based on the Poisson probability function with an expected inhaled dose μ_D :

$$\text{Infection Risk} = 1 - \exp(-\mu_D)$$

- This is the traditional Wells-Riley model for airborne infection.

The Expected Inhaled Dose

The expected deposited dose in the lungs:

$$\mu_D = C_A \times B \times T \times f$$

C_A = concentration in air (# per m^3)
B = breathing rate (m^3 per hour)
T = exposure duration (hour)
f = fraction deposited

Hypothetical Example - Smallpox

Let $C_A = 1\ m^{-3}$, $B = 1\ m^3\ hr^{-1}$, $T = 1\ hr$

Consider 1 – 5 μm particles such that $f = 0.3$

$$\mu_D = 0.3$$

$$\text{Infection Risk} = 1 - \exp(-0.3) = 0.26$$

Respirators and Infection Risk

- A respirator permits some penetration P (0 to 1) due to faceseal leakage:

$$\text{Infection Risk} = 1 - \exp(-\mu_D \times P)$$

- A respirator reduces the expected inhaled dose and, in turn, reduces infection risk.

Hypothetical Example - Smallpox

- For the N95 mask, the assumed value of P is 0.1 (10% leakage). For $\mu_D = 0.3$:

  Infection Risk = $1 - \exp(-0.3 \times 0.1) = .03$

- Is 3% an acceptable infection risk? Public health agencies (federal and State) have not addressed this issue for HCWs.

Is There a Better Respirator Available?

Yes. Tests of high-quality hooded powered air-purifying respirators (PAPRs) used in the pharmaceutical industry show that a typical P = .001 (0.1% leakage) or less.

Cohen, Hecker, Mattheis, et al. (2001): Simulated workplace protection factor study of powered air-purifying and supplied air respirators. *Am. Ind. Hyg. Assoc J. 62*:595-604

Hypothetical Example - Smallpox

- For a hooded PAPR with HEPA filter, the assumed value of P is .001 (0.1% leakage). For $\mu_D = 0.3$:

$$\text{Infection Risk} = 1 - \exp(-0.3 \times 0.001) = .0003$$

- Is .03% an acceptable infection risk? Maybe not, but it's 100-fold lower than 3%.

The Risk-Based Approach

To choose an appropriate respirator, one needs to specify:

- the airborne pathogen concentration
- exposure duration or frequency
- the infectious dose model (deterministic vs. probabilistic) and model parameters
- the respirator Penetration value
- the acceptable risk of infection

The Risk-Based Approach

The greatest sources of uncertainty are:

- **the infectious dose model (threshold vs. probabilistic) and the model parameters**
- **the pathogen concentration in air**

Alternative Infectious Dose Models

- A person must receive X number of microbes to be infected:

$$\text{Infection Risk} = \Pr(\text{Dose} \geq X)$$

- Each microbe has success probability p of infecting. If the Dose is N microbes:

$$\text{Infection Risk} = 1 - (1 - p)^{N}$$

What Is Known?

In general, little is published about the infectious dose of airborne pathogens or the best infectious dose model, but:

- **for *M. tb* bacilli, the evidence overall is consistent with a deterministic infectious dose of one bacillus.**

- **for variola virus, the evidence overall is consistent with a deterministic infectious dose of one virus.**

The Expected Dose of Respirable Pathogens due to a Single Release

- For a single short emission event, estimate the number of microbes N_0 released into air and carried by respirable particles (diameters < 10 μm).

- Estimate the room volume V (m^3), the room supply/exhaust air rate Q (m^3/min), and exposure duration T (min).

The Expected Dose of Respirable Pathogens due to a Single Release

- **The estimated expected dose is:**

$$\mu_D = \frac{N_0}{Q \times T}\left(1 - \exp\left(-\frac{Q \times T}{V}\right)\right) \times B \times T \times f$$

- **If the exposed person is near the emission point (within 3 feet), multiply by 2 or 3.**

The Expected Dose of Respirable Pathogens due to Ongoing Emission

- For ongoing emission, estimate the emission rate E (# per hr) into air of pathogens carried by respirable particles.

- Estimate the room volume V (m^3), the room supply/exhaust air rate Q (m^3/hr), and exposure duration T (hr).

The Expected Dose of Respirable Pathogens due to Ongoing Emission

- **The estimated expected dose is:**

$$\mu_D = \frac{E}{Q} \times B \times T \times f$$

- **If the exposed person is near the emission point (within 3 feet), multiply by 2 or 3.**

Emission Rate in Respiratory Particles

The respirable pathogen emission rate E is the product of:

- **cough rate W (# per hr)**
- **respirable volume per cough V_{RESP} (mL)**
- **pathogen concentration in respiratory fluid C_F (# per mL)**

$$E\ (\#\ hr^{-1}) = W \times V_{RESP} \times C_F$$

The Cough Rate W

Pulmonary TB:	**50% > 3 per hr**
(96 cases)	**8% > 24 per hr**
Pneumonia:	**60% > 12 per hr**
(48 cases)	**29% > 24 per hr**

Loudon and Roberts (1967): Cough frequency in patients with respiratory disease. *Am. Rev. Resp. Dis. 96*:1137-1143

Respirable Particle Volume

In a single cough, the initial volume in particles with final diameters ≤ 10 μm is:

$$V_{RESP} = 6 \times 10^{-8} \text{ mL}$$

Nicas, Nazaroff and Hubbard (2004): Toward understanding the risk of secondary airborne infection: emission of respirable pathogens, *J. Occup. Environ. Health*, in press

Inspirable Particle Volume

Particles with diameters 10 μm to 100 μm are inhaled but do not reach the alveolar region. In a single cough, the initial volume in particles with final diameters 10 μm to 100 μm is:

$$V_{INSP} = 14{,}000 \times 10^{-8} \text{ mL}$$

Nicas, Nazaroff and Hubbard (2004): Toward understanding the risk of secondary airborne infection: emission of respirable pathogens, *J. Occup. Environ. Health*, in press

M. tuberculosis C_F Values

For a series of 22 pulmonary TB patients, the concentration of viable *M.tuberculosis* bacilli in sputum was assayed:

- **mean: 8.4×10^6 per mL**
- **range: 6.6×10^4 to 3.4×10^7 per mL**

Yeager, Lacy, Smith and LeMaistre (1967): Quantitative studies of mycobacterial populations in sputum and saliva. *Am. Rev. Resp. Dis. 95*:908-1004

M. tuberculosis Example

- Using the median cough rate $W = 3\ hr^{-1}$ and mean concentration $C_F = 8.4 \times 10^6\ mL^{-1}$

$$E = 1.5 \text{ respirable bacilli per hr}$$

$$(3\ hr^{-1}) \times (6 \times 10^{-8}\ mL) \times (8.4 \times 10^6\ mL^{-1})$$

- A classic study by Riley, et al., found the average emission rate of respirable *M. tuberculosis* bacilli was 1.2 per hour.

Superspreaders and Dangerous Disseminators

- These highly infectious source cases likely have high values for cough frequency, pathogen concentration in respiratory fluid, and aerosol volume per cough.

- These source cases appear infrequently, but they usually cannot be identified beforehand and they are certain to show up eventually.

What If Pathogen Exposure Cannot Plausibly Be Estimated?

- In a laboratory setting, it is difficult to estimate the volume of culture fluid that would be aerosolized or the particle size distribution.

- Other than for *M. tuberculosis*, data on pathogen concentrations in respiratory fluid are not published, and there can be great variability in C_F among patients.

Respirator Selection in the Face of Uncertainty

- I suggest a conservative approach.
- Assume that the infectious dose is one microbe (unless there is good evidence to the contrary).
- Assume that the expected dose without respirator use over the duration of exposure will equal one microbe (unless there is good evidence to the contrary).

Respirator Selection in the Face of Uncertainty

- Given these assumptions, the risk of infection without respirator use is 63%.
- An N95 filtering-facepiece respirator should reduce infection risk to 9.5%. A hooded PAPR with HEPA filter should reduce infection risk to 0.1%.
- Use a hooded PAPR with HEPA filter.

Respirator Selection in the Face of Uncertainty

- Regardless of the final selection, the decision process should be documented with assumptions identified, a numerical risk estimate offered, and an acceptable risk level specified.

- I suggest not relying on someone else's expert opinion if the assumptions and acceptable risk values are not defined.