

NIOSH Diacetyl REL Hearing slides

David Egilman MD, MPH
Clinical Associate Professor
Department of Family Medicine
Brown University
degilman@egilman.com

Hank Schilling BS works for Dr. Egilman

Dr. Egilman has served as a consultant at the request of workers exposed to diacetyl who were seeking compensation for injuries in worker compensation and tort lawsuits. He was not compensated for work or expenses related to this presentation

Surveillance System

Let's not repeat this mistake again

Establish registries with standard occupational and environment questionnaires with:

1. Lung transplant units
2. Liver transplant units

For these workers:

- Set up a registry for cases
- Work with NIH to set up treatment protocols

REL based on highest exposure

- REL is based on Company G analyses (pg 138).
Excess risk of 1/1000 at:
 - 3-5 ppb** (all workers)
 - 5 ppb** (smokers)
 - 0.9 ppb** (non-smokers)
- Company K/L (pooled) 1/1000 at **0.4-0.5 ppb** (all workers) (pg. 138)

Multiple RELs?

- “Excess risk of 1/1000 corresponds to approximately 0.003–0.005 ppm diacetyl (10.5-17.5 $\mu\text{g}/\text{m}^3$) in the general population and **0.0009 ppm (3.15 $\mu\text{g}/\text{m}^3$) for non-smokers.**” (page 138:7-8)
- Exposure level should be based on protecting most sensitive group (non-smokers)
- Standard should be set at **< 1 ppb ALARA**

UNPRECEDENTED and WRONG DOUBLE STANDARD

- NIOSH has never set different standards for smokers and non-smokers
- In this case NIOSH chooses to ONLY protect smokers

THE TLV SHOULD PROTECT ALL
WORKERS NOT JUST SMOKERS

QSAR analysis

- Qualitative structure-activity relationship performed by ToxDx for ConAgra
- Compares LUMO (lowest unoccupied molecular orbital) values between diacetyl, 2,3-pentanedione and other known lung toxins
- Negative LUMO values indicate high biological reactivity and toxicity potential
- Similar LUMO values indicate similar toxicity

QSAR analysis

- “Of particular note is that only two of the butter flavor chemical constituents exhibit negative LUMO energy values, indicative of chemicals with greater reactivity and greater potential of causing chronic irritation. Both are di-ketones, diacetyl and 2,3-pentanedione.”
- “Three isocyanates were also included in the data set because of their well-established reputation for inducing allergenic bronchiolar asthma. Of note is that the calculated LUMO energy values are similar to those calculated for diacetyl and 2,3-pentanedione.”

ToxDx Report. Consumer Safety Estimate for Inhalation of Synthetic Butter Flavoring Components of Microwave-Ready Popcorn. Submitted April 21, 2005 by Kendall Wallace, Ph.D., DABT

QSAR analysis

- Toluene-2,4,-diisocyanate (TDI), diacetyl and 2,3-pentanedione have comparable LUMO values and therefore comparable reactivity and toxicity.
- ACGIH states that it intends to reduce TLV for TDI from 5 ppb to **1 ppb**¹

¹ ACGIH. Toluene-2,4- or 2,6-Diisocyanate: TLV[®] Chemical Substances Draft Documentation, Notice of Intended Change. Publication #7NIC-140

Other chemicals

- “Although a causative relationship between diacetyl and respiratory disease has been observed, diacetyl may not be the only flavoring ingredient related to health impairment. Other flavoring ingredients such as acetaldehyde, butyric acid, and acetoin, have been associated with adverse health effects [Lockey et al. 1998; van Rooy et al. 2007]” (page 12:11-12:14)

Other chemicals

- Acetaldehyde, butyric acid, and acetoin are not associated with BO
- Key issue is whether these chemicals impact effective dose, i.e. toxicity of diacetyl to induce BO

Butyric acid

- “For example, butyric acid, one of the vapors present in butter flavoring vapors, is a known inhibitor of an enzyme that metabolizes diacetyl. **Currently it is not known if an inhibition of this enzyme would diminish or enhance the effects of diacetyl.**”
 - Dr. Morris expert report, Newkirk vs. ConAgra

Butyric acid

- Morris & Hubbs (2008) results suggest butyric acid enhances diacetyl penetration to lower airways (in rats)
 - Site of injury to humans
- Butyric acid may also enhance diacetyl toxicity by inhibiting detoxification enzyme

NIOSH denies consumer risk

“The CDC’s National Institute for Occupational Safety and Health (NIOSH), Environmental Protection Agency, and the Food and Drug Administrations **say there is no reason for consumers to worry.**

‘We don’t see any evidence for consumer risk,’ NIOSH spokesman Fred Blosser tells Web MD.”

<http://webmd.com/news/20040312/microwave-popcorn-no-consumer-risk-known>

Posted 3/12/2004
9/29/2011

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NIOSH denies consumer risk

“Workers often have different exposure characteristics, including level of exposure, to flavorings than typical consumers. Unlike workers, so far there have not been peer reviewed scientific studies showing that consumers using products such as microwave popcorn that contains butter flavoring chemicals are at increased risk of lung disease. Nor is there any evidence that cooking with butter is associated with increased risk for lung disease...

Currently, even though there is little to suggest significant risk to normal consumers...”

http://www.cdc.gov/niosh/blog/nsb111008_diacetyl.html

9/29/2011
Posted 12/4/2008

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FDA denies consumer risk

“The FDA classifies diacetyl as being "generally recognized as safe." Last September, the FDA received a citizens' petition to revisit diacetyl's safety status. An FDA spokesperson says the FDA isn't aware of any evidence that consuming diacetyl is unsafe.”

<http://www.webmd.com/lung/news/20080313/kernel-of-truth-about-butter-flavoring>

Posted 3/13/2008
9/29/2011

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Consumer exposures exceed NIOSH recommended exposure

- Jasper GML plant: QC worker's breathing zone exposure as bag of popcorn is opened reached peak of **4, 7, and 13 ppm** (FTIR method)

Figure 4. Diacetyl and acetoin air concentrations in the quality control room.

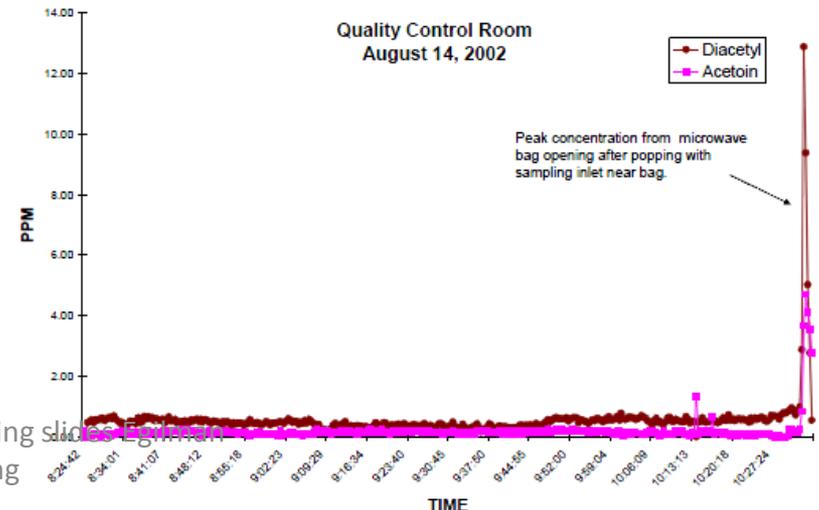
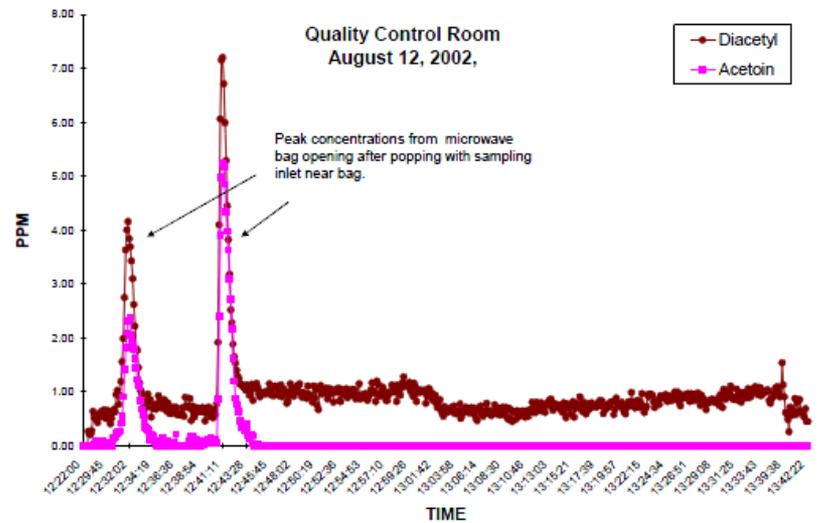
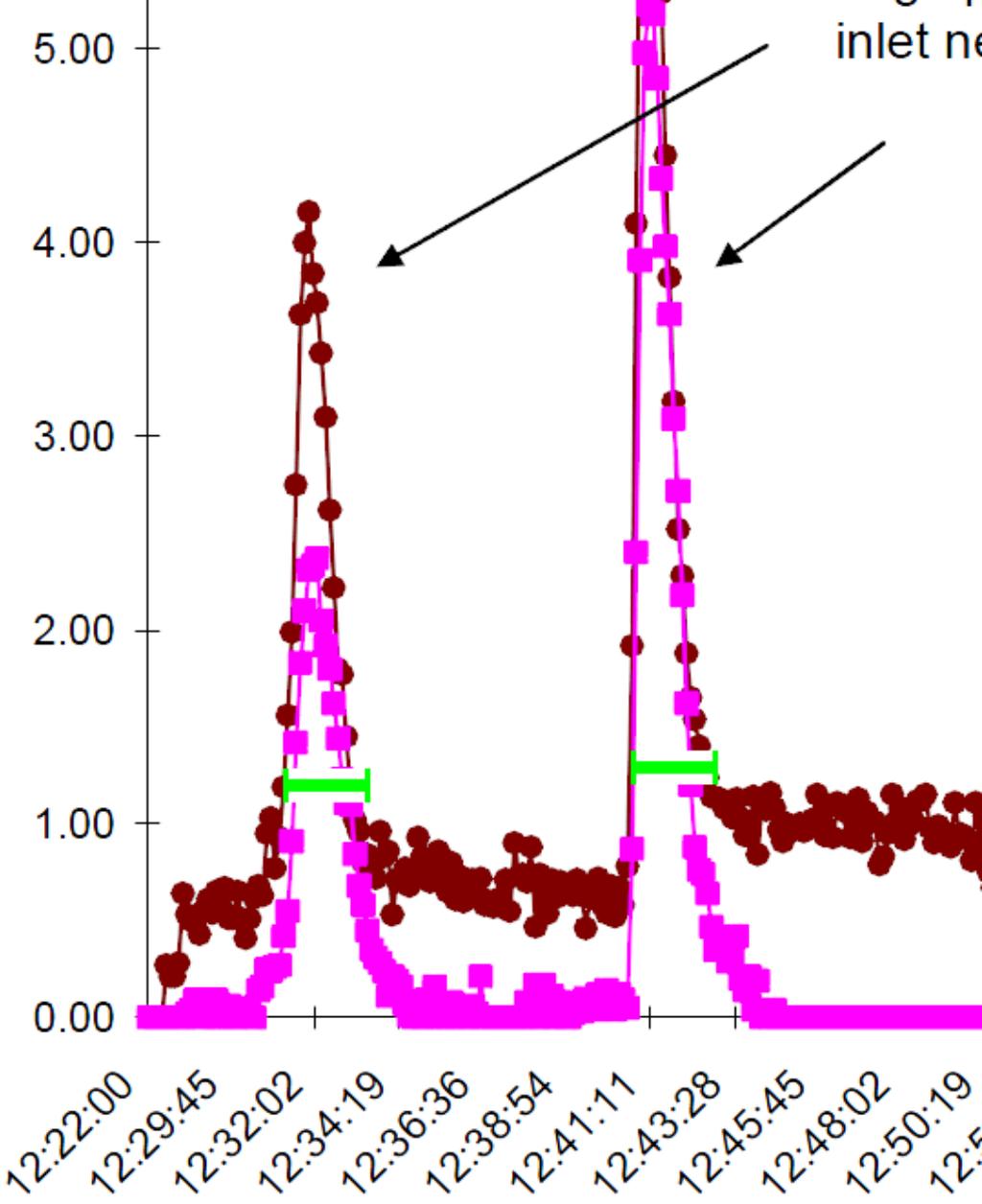


Figure 4, page 28 NIOSH GML HHE

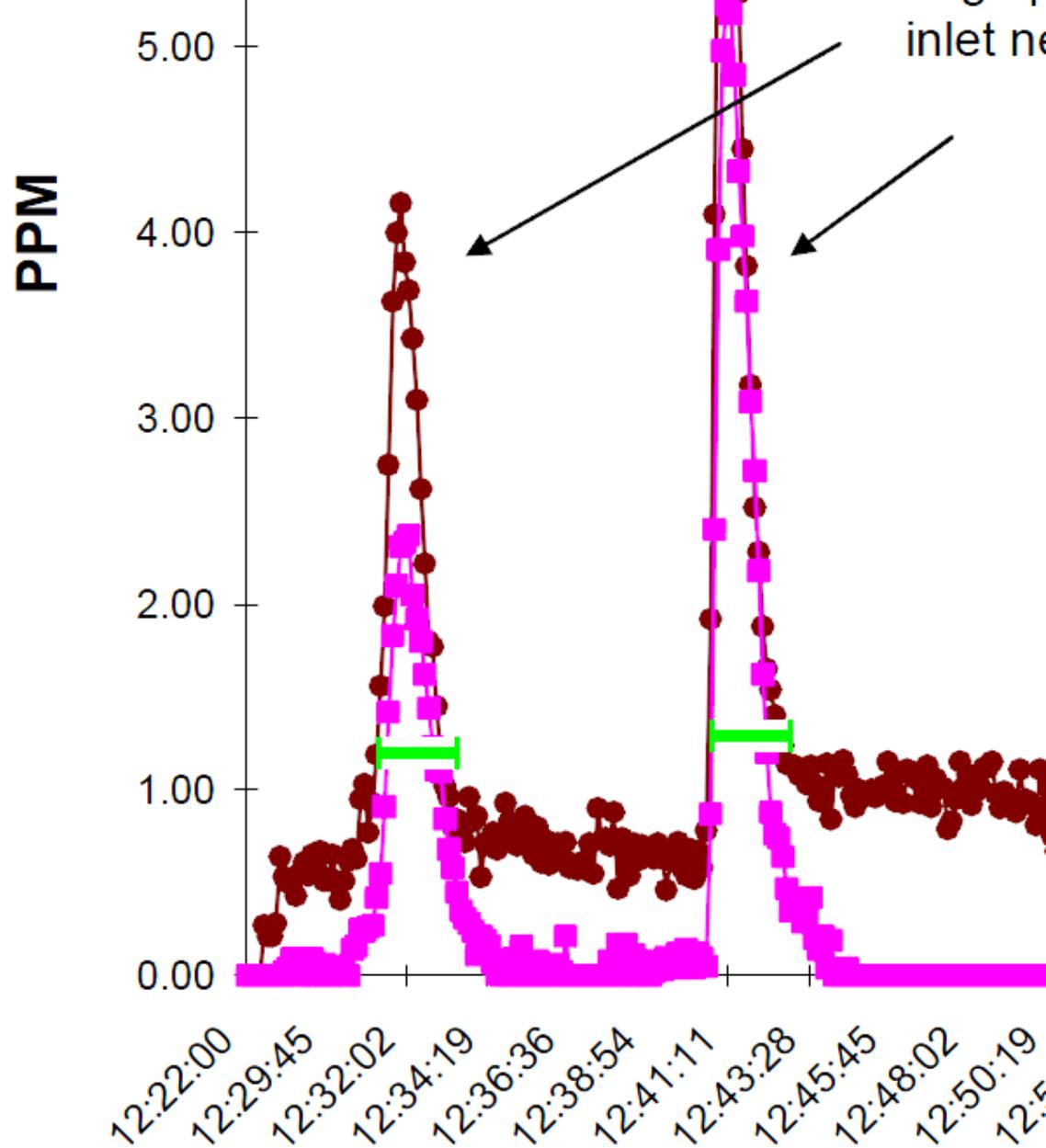
- Diacetyl levels from opening one popcorn bag remain above background levels for **over two minutes**



2:17 minutes



- 15 sec exposure at peak level for each bag is conservative estimate
- Actual exposure could be determined by taking area under peak curve



Consumer exposures exceed NIOSH recommended STEL per bag

- NIOSH STEL: **25 ppb** over 15 min
- Assuming peak exposure for 15 sec/bag:
 - 4 ppm over 15 sec = **67 ppb** over 15 min
 - 7 ppm over 15 sec = **117 ppb** over 15 min
 - 13 ppm over 15 sec = **217 ppb** over 15 min

Consumer exposures can exceed NIOSH REL

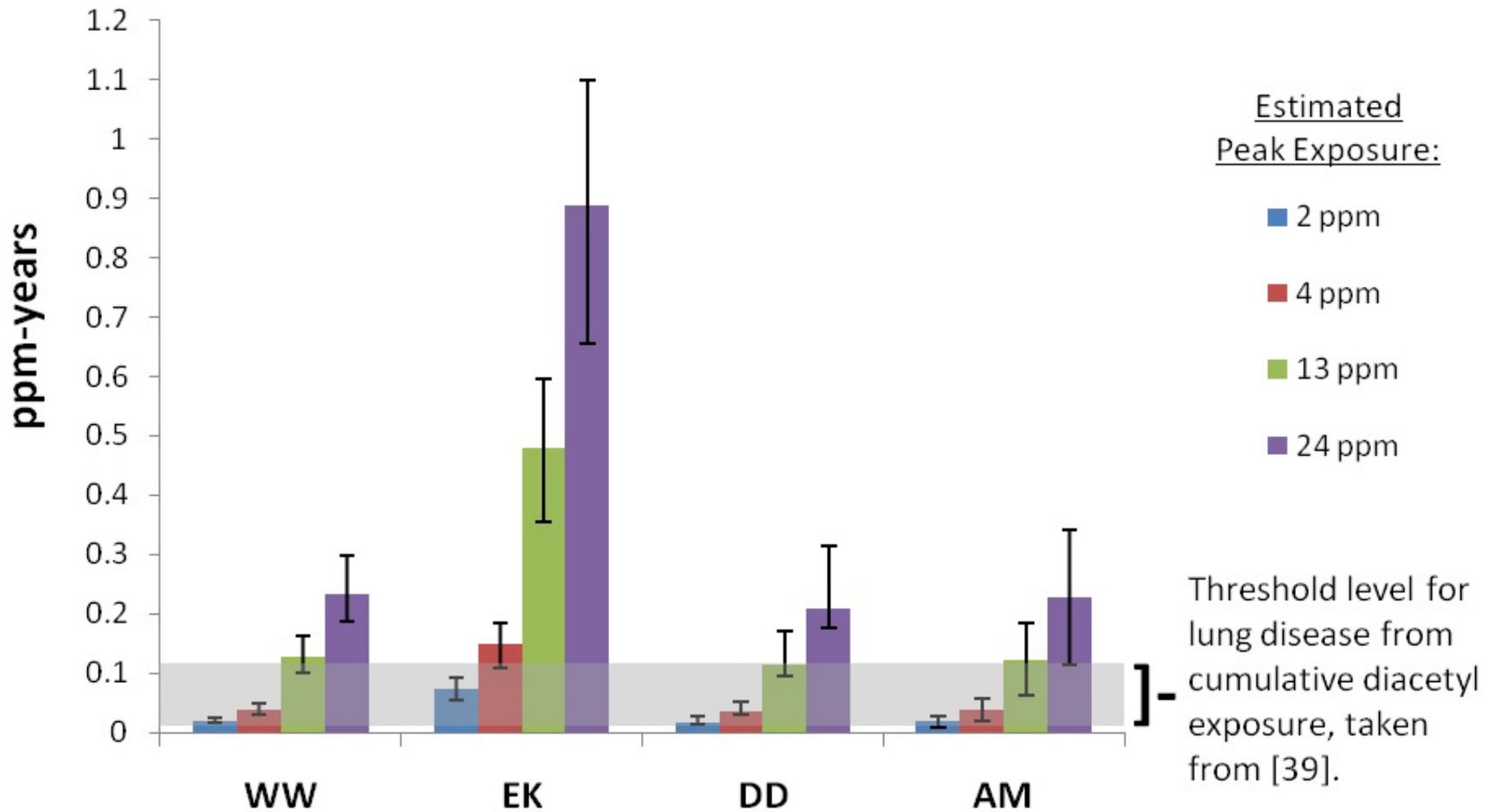
- NIOSH REL: **5 ppb** for 8-hour day
- Assuming peak exposure for 15 sec/bag:
 - 4 ppm: **3 bags/day = 6.2 ppb** 8-hour TWA
 - 7 ppm: **2 bags/day = 7.3 ppb** 8-hour TWA
 - 13 ppm: **1 bag/day = 6.8 ppb** 8-hour TWA

Known consumer cases of BO

Case	Biopsy confirmed BO?	Smoking History	Consumption level
WW	Yes	None	1-3 bags/day, 8 years
EK	Yes	None	3-5 bags/day, 8 years (home) + 30 bags/weekend, 4 years (work-related)
DD	Yes	None	2-3 bags/weekday, 7 years
AM	Yes	None	2-3 bags/day, 7 years

- Differential diagnosis found no other cause of BO in any case

Cumulative Exposure Estimates



Error bars represent range of consumption estimates.

24 ppm (purple bar) comes from Aspen study: peak of 372 ppm (Orville Redenbacher Butter), converted to 46 L breathing zone.

Lockey et al. (2009) PAPR mixers

- Mixers using PAPRs at 5.7-fold increased risk for obstruction
- Maximum 3 years exposure
- Lockey estimated average exposure level of 0.015-0.044 ppm
 - Measured levels / 25
 - (“conservative resp. protection factor”)
- Cumulative exposure: 0.045 – 0.132 ppm
- → 8-hour TWA: **1 to 2.9 ppb (unsafe)**

Wrong Odor Threshold in Air

- Table 1.1, page 16
- Diacetyl (Illovo Sugar Limited 2009):
 - NIOSH draft: Table 1.1 says **0.09 ppb**
 - In fact, it is $0.09 \text{ mg/m}^3 = \mathbf{25 \text{ ppb}}$
- Diacetyl and 2,3-pentanedione (Blank et al. 1992):
 - Table 1.1 says **0.01-0.02 ppb**
 - In fact, it is $10 \text{ to } 20 \text{ ng/L} = \mathbf{2.8 \text{ to } 5.6 \text{ ppb}}$

Odor Threshold in Water

- Table 1.1, page 15
- Diacetyl (Diaz et al. 2004): 0.05 ug/L = **14 ppb**
- Lawless et al. (1993): 0.005 ug/mL = **1.4 ppm**
 - “Individual thresholds varied over a factor of 256”

$$\frac{ug}{L} = \frac{ppmV (12.187)(MW)}{T}$$

Equivalent units:

$$ug/L = ng/cc = mg/m^3$$

Odor Threshold

- NIOSH Table 1.1 states odor threshold in air is far below recommended exposure level
- In fact, odor threshold in air and water is above dangerous level
- Thus, diacetyl does not have an odor warning property