Allergens in the Workplace: A Case Study of Animal Allergens and the Development of an Occupational Exposure Limit

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Clinical Case Example

- Hx: 25 yo staff biologist working primarily with rodents. Over past 3 months, developed increasingly severe upper respiratory allergic symptoms (sneezing, nasal congestion, watery eyes) whenever works with rodents. Denies rash, wheezing, or history of asthma. PPE – surgical mask.
- Allergy Test Results:
  - Skin Testing- suggestive of rat allergy
  - RAST Testing: Positive for Rat Urine and Cat Dander
- Disposition:
  - Treated short term with nasal steroids, antihistamine, removal from exposure to rat at work
  - Final Disposition: permanently restricted from work with rats
LAA - Introduction

- POPULATION AT RISK: Workers exposed to furred lab animals – resulting condition termed Lab Animal Allergy (LAA)
- LAA - a major Occupational Illness to:
  - technicians,
  - animal caretakers,
  - veterinarians,
  - physicians
  - scientists
- Goodno and Stave, in JOEM, 2002, - 125,000 workers in U.S., and 15,000 in U.K. regularly work with laboratory animals,
  - 33% may develop symptoms of LAA
- Wolfle and Bush, in Institute for Laboratory Animal Research (ILAR)
  - 46% of lab animal workers will develop allergic symptoms, and of those, more than 10% develop Occupational Asthma
- NIH-Manifestations of LAA cause more than one third of lab animal workers to lose time from work.
- Lab Animal Allergy= important health problem for animal workers, and an administrative and financial burden on the research institutions due to lost productivity and health care costs.
Epidemiology – cont’d

- **Prevalence** – Goodno and Stave- cross sectional studies estimate prevalence of LAA to be as high as 44%
- **Incidence** – estimates range from 10% - 37%
- **Cullinan et al**
  - Mean duration of employment before symptoms to rat exposure
    - Respiratory = 365 days
    - Nose and eye = 214 days
    - Skin = 335 days
- **Animals and allergenicity** –
  - many authors report mice and rats are most allergenic
  - **Bush, Wood, and Eggleston** report in *J Allergy Clin Immunol* that allergy to other animals in the workplace is less common than allergy to rats and mice **primarily because other animals are used less**

- In a large Japanese epidemiologic study, allergy symptoms reported in:
  - 26% workers exposed to mice or hamsters
  - 25% for rats or dogs,
  - 31% for Guinea Pigs,
  - 30% for rabbits or cats, and
  - 24% for monkeys.
Epidemiology (cont’d)

- Risk of LAA is in part due to **activity** of worker – cage cleaning exposes worker to higher airborne allergen level than other activities.
- LAA is preventable – Goodno and Stave – 2002 study – reduced exposure with PPE led to LAA incidence of zero.
- Secondary LAA - Goodno and Stave reported in JOEM Dec 2002 that for those workers with primary LAA who remained in the workplace, up to 8% developed allergy to a second species (10 year Secondary LAA Incidence rate =11(95% CI, 7.4 -14.6) cases per 100 person- years.)
SCOPE

- **Source of animal allergens** – animals shed allergens through *urine, dander, hair, serum, and saliva*,
  - but not all species or strains do so equally
- **Gender inequity** – in general, females shed fewer allergens than males
- **Allergen exposure related to:**
  - Size of allergen particle
  - Environmental conditions in cage
    - Type of bedding
    - Density of animals
    - Ventilation of rooms
  - Job/task responsibility
  - Duration of exposure
The Allergens

- Belong to family of proteins called **lipocalins**
- Lipocalins - produced in **liver** or **secretory glands**
- Lipocalins share biological and structural properties that elicit similar responses from the human immune system
- Proteinuria in rodents - persistent proteinuria results in urine as major source of allergen production and worker exposure

- Other rodent sources of allergens - hair, dander, saliva (less allergenic)

- Cats and dogs - hair, dander, and saliva all major sources of allergen production
The Allergens-Mouse

- **Mus m 1** - pre albumin protein, molecular weight 19 kd
  - Gene molecularly cloned, and amino acid sequence has been deduced
  - Mus m 1 found in urine, hair follicles, and dander
  - Produced in liver cells
  - Levels in serum and urine are four times higher in male mice compared to females
    - Due to testosterone dependence of gene expression

- **Mus m 2** – glycoprotein, molecular weight 16 kd
  - Originates in hair follicles and dander
  - Not found in urine

- **Albumin** – third major allergen
  - Found to be allergenic in 30% of individuals exposed to mice
The Allergens – other animals

- **Rats** –
  - When produced in **liver** – androgen dependent
  - When produced in **exocrine glands** (salivary, mammary, meibomian, preputial), not androgen dependent

- **Rabbits**

- **Cats**
  - Minimum 12 proteins of cat origin found to be allergenic
  - Fel d 1 most allergenic by far
  - Molecular weight 38kd
  - Produced in hair follicles and to lesser extent saliva
  - Male cats produce more Fel d 1 than females

- **Dogs**
  - Can f 1, most important Dog allergen
  - Polypeptide, molecular weight 25kd
  - Produced in hair follicles, dander, ad saliva

- **Other**
  - Non-human primates – conflicting data
Environmental Distribution

- Animal allergens carried on relatively small particles
  - Studies show airborne mouse allergen particles range from 3.3 to 10 microns in one study, 6-18 microns in second study

- Small particles can remain airborne for extended periods of time, and are easily respirable

- Airborne mouse allergen studies
  - Levels range from 16.6 to 563 ng/m3 in rooms with mice and from 1.2 to 2.7 ng/m3 in rooms without mice
  - Another study showed airborne levels ranged from 1.8 to 825 ng/m3, and varied with number of mice and degree of work activity in room
  - Another study showed higher allergen levels in rooms with male mice compared to rooms with female mice (Mus m 1, 13,050 pg/m3 vs. 317 pg/m3)

Airborne rat studies also showed levels highly dependent on type of activity being performed
- cleaning and feeding associated with highest levels of exposure
Mechanism of LAA

- Activation of innate immune response pathways by bioaerosols such as animal allergens, endotoxins, peptidoglycans, and B-glucan
  - Pathogen-associated molecular pattern (PAMP) recognition molecules (e.g., toll-like receptors (TLRs))
  - Initiation of inflammatory responses
  - Initiation of adaptive immune response

- Laboratory Animal Allergy – **Type 1, immediate hypersensitivity reaction** according to Gel and Combs
  - Involves production of Immunoglobulin (IgE) antibodies formed in response to protein LAA antigen
  - CD4+ T – helper lymphocytes play central role in generation of IgE antibodies
  - LAA exposure occurs primarily through inhalation of allergen proteins
  - Skin contact a minor exposure route
Development of IgE Antibodies

- **Sensitization** – development of IgE antibodies to the specific allergen

- Allergenic protein taken up by *Antigen-Presenting Cells (APC)* Lung APCs
  - Monocytes
  - Alveolar macrophages
  - Dendritic cells
- Skin APCs
  - Langerhans cells
  - Dendritic cells
Development of IgE Abs

- Antigen - processed into small peptide fragments and presented on the surface of APC in association with Major Histocompatibility (MHC) class II molecules
- Naïve T Cells recognize the complex of the MHC molecule and the allergenic antigen
- With this recognition signal, and other costimulatory signals (B7 and CD28 interaction), T cell becomes activated
- Activated T cell undergoes multiple rounds of replication under effect of the cytokine Interleukin 2 (IL2)
- Result is multipotential population of T cells (Th0)
Th0 T cells serve as progenitors of two different types of Effector Cells-
- Th1 lymphocytes – develop in presence of IL12 and Interferon gamma (IFNg)
- Th2 Lymphocytes – develop in presence of IL4

Th1 cell produces IFNg, which suppresses the formation of IgE antibody production

Th2 response is the typical feature of immediate-type allergic diseases
- The production of cytokines (IL-4, IL-13) stimulates B Lymphocytes to produce antibodies specific to the allergen presented

Subsequent exposure (even years later) to the initial sensitizing allergen elicits a rapid and vigorous response
Allergy mechanism – cont’d

- **PREDISPOSITION** – for many allergic diseases, a genetic predisposition (Atopy) is present
- Individuals are defined as being atopic if they, or close relatives, have manifestations such as
  - Allergic rhinitis
  - Asthma
  - Eczema
- **Current theory of allergy** – lack of production (or imbalance) of IFNg vs IL4 and IL13 in atopic individuals causes production of IgE to allergenic protein
- Intended role of IgE in human health – unknown
  - May be related to body’s response to Parasitic infections
  - IgE production causes recruitment of Eosinophils, which have been shown to kill parasites such as schistosomes in culture
- **Role of IgE antibody in allergy** – binds to Fc receptors on mast cells and basophils
- **Causes release of chemical mediators of allergic symptoms in these cells in:**
  - Respiratory tract,
  - GI tract,
  - Skin,
  - Conjunctiva
Sensitization / Allergy Mechanism (ILAR 2003)
Development of Allergic Symptoms

- Early Phase Reaction –
  - Specific allergen interacts with IgE antibodies on surface of mast cell or basophil
  - Results in release of preformed biochemical mediators
    - histamine,
    - leukotrienes,
    - activation of arachidonic acid cascade causing production of prostaglandins,
    - generation of cytokines (TNF-a, IL-1, IL-4, IL-5, IL-6, IL-8, & IL-16)
    - and generation chemokines (MIP-1a, MIP-1b, MCP-1, and RANTES)

Resulting pathophysiology -
- tissue edema (nasal congestion, bronchial edema, hives)
- increased mucous secretion (rhinitis, bronchi)
- nerve stimulation causing itching (skin, eyes), sneezing, bronchospasm
- systemic allergic reaction (anaphylaxis) – pruritus, urticaria, angioedema, edema of larynx, acute asthma, hypotension and shock
Medical Surveillance

The major objective for **health** and **safety** = eliminate and reduce exposures (*Primary Prevention*). Examples:

- Reducing the use of use of animals in experimentation
- Controlling the environment in the animal facility to reduce exposures
- Limiting the number of personnel with access

**Medical surveillance** is *Secondary Prevention* – *purpose is to identify early signs of disease, hopefully at a stage in which intervention will improve the outcome*

**Basis for Medical Surveillance program** – no formal legal requirement (OSHA)

- Ethical responsibility of employer to minimize disease risk & burden on employees
- Good business to prevent disease in employees

**Elements**

- Preplacement testing- limited in value due to lack of predictive value for developing LAA
- Baseline History- useful as baseline for changes in future- also identifying higher risk individuals to watch closely for S/S early allergic disease
- Periodic questionnaires with appropriate follow-up(physical exam, testing) of changes to facilitate early identification of allergy
- Education of lab animal workers on risks, signs and symptoms of interest valuable
- Statistical analysis of population data to detect trends
ASSESSMENT

- History of symptoms in conjunction with exposure
  - Nose - chronic congestion and rhinorrhea, sneezing, pruritic nose and throat
  - Skin - eczematous rash (scaly, pruritic, red rash in flexural areas of arms and legs)
  - Lungs - wheezing, cough, chest tightness, SOB; occurring episodically, especially after allergen exposure, exercise, irritants such as smoke, URIs

- Tests for IgE-mediated allergy
  - Skin testing
    - Drop of allergen extract is placed on skin, which is pricked with small lancet
    - Diameter of wheal and flare that result within 15 minutes is measured and compare to histamine control
  - RAST Testing
    - Allergen binding by IgE antibody, if present, is detected by second antibody
  - Both tests correlate; RAST is more expensive and not affected by medications, but less sensitive
  - Both tests are dependent on composition of extract of allergen
    - Concentration of allergen extracts of different lots of same allergen can vary by as much as 1,000 fold
    - Concentration of allergenic proteins decreases with time due to proteases present
    - Standardized, stable extracts for ANIMAL allergens are very limited

- Clinical Testing
  - Pulmonary Function Testing (daily peak flows – looking for changes 15%, cross-shift spirometry looking for changes in FEV1 and FVC after exposure, Methacholine Challenge Testing, Specific Inhalational Challenges)

- Genetic Testing (HLA-B16 an HLA-DR4 association with animal allergy risk?)- Utility?
TREATMENT

- Emergency treatment of anaphylactic reactions (epinephrine, ACLS system)
- Exposure reduction / avoidance
  - administrative controls
  - Improve Engineering controls
  - Change Lab animal care practices
  - PPE
- Corticosteroids (topical, oral, inhaled, IV)
- leukotriene receptor antagonists
- Antihistamines
- Inhaled Beta Agonists
- Immunotherapy
  - Immunotherapy to cats and dogs successful in a few reports, but only in workers intermittently exposed rather than chronically exposed
  - Uncontrolled studies of immunotherapy to lab animals (mice, rats, and rabbits) have demonstrated some improvement
  - Insufficient study to recommend immunotherapy as a means to protect workers from developing symptoms with exposure
- Risk of treating with continued exposure
  - Asthma development risk – 3-6% of 1 LAA
  - Secondary LAA development - (Goodno & Stave, Hazard Ratio (HR) for developing 2 LAA =8.21
    
    95% CI, 7.33-8.83, P < 0.001)
CONVENTIONAL WISDOM: no clearly established threshold for allergen exposure supports a minimum safe exposure level

Goal: Defy CW & Establish a Working Exposure Limit
ANIMAL ALLERGENS (AA) & ENDOTOXINS
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A RECOMMENDED CONTROL STRATEGY

Terry Lane & Dr. Pete Nigro
Selection of AA Exposure Limit

- Clear exposure-response relationship at ~100 ng/m$^3$
  - ~ 2.5-4X risk of + skin prick test & chest symptoms$^1$

- Clear exposure response relationship between RUA exposure & specific IgE antibodies to lab rat allergens
  - Exposure-response relationship robust$^2$

- Suarthona et al in AJIM 2005: “Exposure level to High Molecular Weight allergens is strong predictor of sensitization”

$^1$Nieuwenhuisjen M., et. al, JOEM, 1999: 60
Dose-response relationship

- 1990, Eggleston and Ansari reported 12 volunteers symptoms with exposure for one hour to Rat n 1 levels ranging from 1.5 ng/m³ to 310 ng/m³.
- All 12 (100%) experienced nasal symptoms by end of one hour exposure.
- 5 of 12 (42%) showed decrease in FEV1 over 10% within one hour exposure.
- In a follow up study, high allergen levels (cage cleaning, mean Rat n 1 = 166 ng/m³) were compared to low allergen exposure levels (quiet sitting in rat vivarium, mean Rat n 1 = 9.6 ng/m³) in 17 subjects.
  - A clear dose-response was demonstrated with both upper and lower airway responses being dependent on airborne allergen levels.
Discussions with G. Evans & HSL peer review experts
- Health / exposure data
- Peak vs. TWA comparisons

Institute of Occupational medicine (2005)–
- Carried out studies on correlation of airborne concentrations of mouse and rat urinary proteins vs. allergic response
- Concluded concentrations above 6 ng/m3 increased likelihood of sensitization

Nieuwenhuijsen et al in *Occ & Env Med* 2003, as well as Pacheco et al, in 2006 *Annals Occupational Hygiene* – “peak exposures more important than mean exposures in triggering sensitization
Literature supporting AA exposure limit

- Hollander, Heederik & Doekes – 1997 Am J Respir Care Med
  - reported prevalence rate of sensitization to lab animal allergens clearly associated with exposure levels
  - Clearest association with “high level exposure” at 4.2 ng/m3

  - Environmental exposure challenges performed to find allergic threshold concentration
  - Found statistical correlation between exposure concentration and allergic mediator release
  - Significantly smaller allergic responses with exposures below 10 ng/m3
AA Exposure Limit

- S. Gordon (formerly IOM) recommended maintaining exposures at or below 5 ng/m³
  - Feasible controls for rodent allergens
  - Reduced risk of LAA at this level - study of 458 workers newly exposed workers to MUP
  - Similar reduced risk of LAA to rats anticipated at this level of exposure
  - LAA risk reduced but not eliminated; still risk that a small number of people will develop LAA

Problem Resolution Approach

- Extensive literature review (+ 50 papers)
- Benchmarked with key pharmaceutical companies; obtained other benchmarking data from research institutes
- Formulated Position / Control Strategy
- External peer review of position paper/slides by UK’s Health & Safety Lab (HSL) experts
- Internal stakeholder review - WP LAR & Safety
Setting AA Exposure Limits - Challenges

**Variability LAA Cases**
- (GSK 10-year Study): 
  - Most occur in first 3 years of exposure 
  - At least 36.5% cases did not occur until > 5 years 
  - 9.2% cases occur after 20 years exposure 
  - 33% of workers with 1° allergy (1 species), developed 2° allergy to at least 1 more animal species 
  - Increase incidence of 2° allergy increased to ~ 50% > 10 years; workers more likely to be atopics & some had up to 6 allergies

**Confounding Factors**
- Individual susceptibility – 
  - Subset of population will not develop sensitization regardless of exposure 
  - Increased risk for atopics, +/- smokers 
  - Endotoxin co-exposure

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2. GSK Data – Practical Approaches to Managing OH Programs in Your Animal Facility Conf: 1996
Setting Exp Limit – Challenges (cont’d)

- Choosing endpoint

  - **Allergy**
    - Pro – easy to detect; accepted medical management
    - Con – acting “late” less defensible
      - Goodno, 2002 JOEM – exposure levels against primary LAA not sufficiently protective against secondary LAA
      - Gordon & Preece 2003 *Occ Med* – suggest sensitization to allergens at levels < allergy symptomatic level

  - **Sensitization**
    - Pro – “early” detection can prevent disease progression
    - Con – logistical difficulties in detecting sensitization
      - ? Legality of actions based upon sensitization
Background – Endotoxin Exposures

- Numerous studies linking various health effects (e.g., fever, joint pain, respiratory effects) with exposures to endotoxins

- Key endotoxin exposures from animals & feces

- Co-exposure of AA & endotoxin may be important in development of sensitization
  - Peak exposure vs. mean TWA exposure may be more important in triggering symptoms & immunologic sensitization
  - Chronic exposure may alter susceptibility to sensitization & may reduce the dose at which the allergens can trigger allergic responses

Endotoxin - Health Effects

- Inhaled endotoxins – respiratory & systematic inflammatory responses

- Acute Health Effects (high exposures - e.g., pig farms):
  - Systemic & respiratory
    - Dry cough/shortness of breath, decreased lung function
    - Fever reactions & malaise
    - Occasional dyspnea, headache & joint aches

- Chronic Health Effects:
  - May cause chronic bronchitis & reduced lung function
  - Co-exposure may be important in development of LAA sensitization

Endotoxins – Hazard Assessment

- No Effect Levels – calculated to range from 90 - 1700 EU/m³ (9 – 170 ng/m³)

- Dutch Expert Committee on Occupational Standards recommended a health based OEL-TWA = 50 EU/m³ (~ 4.5 ng/m³)
  - Changed to 200 EU/m³ – to address ‘feasibility’ within agricultural industry
  - Measured as “inhalable dust”
  - Recently changed to 90 EU/m³

Prevention (Cont’d)

- ENGINEERING CONTROLS
  - Material Change / substitution
    - Animals (less allergenic species or strain, juvenile or younger animals, female gender)
    - Bedding (non contact pads or corncobs vs wood chips or sawdust reduces allergen levels in air by 57 – 68%)
  - Ventilation changes to reduce amount of airborne allergens and duration of exposure
    - Filtering air with HEPA filters (local controls)
    - Increased room air exchanges (general dilutional)
  - Filter topped cages
  - Process Change (e.g., automation using robots for cage washing)
  - Isolation / enclosure
  - Exposure limits (peak exposures)
Prevention (cont’d)

- **ADMINISTRATIVE CONTROLS**
  - limiting access to animal care areas
  - limiting animal stock density in rooms
  - limiting duration of work in animal care rooms
  - regular housekeeping such as wet mopping and water-hosing

- **PERSONAL PROTECTIVE EQUIPMENT**
  - Respirator
    - Dust masks approved by NIOSH shown in studies to remove up to 98% of rodent urinary allergens from inhaled air – probably OK for asymptomatic animal care workers
    - Better allergen reduction for asymptomatic, and possibly for symptomatic – ½ face negative pressure respirator, PAPR with hood, or better
    - NOTE: the use of respirators has not been shown to reduce progression of disease and is not a substitute for removing severely allergic individuals from exposure.
  - Gloves
  - Hats
  - Gowns
  - Shoe covers
  - Eye protection
Disposition question: Whether to allow individual with established LAA to continue working using PPE, or to remove from position?

- Studied relation between sensitization and subsequent lung function decline in working populations exposed to allergen(s).
- Method: longitudinal study (median follow up 2.0 years) – 319 lab animal workers- excluded subjects with over 4 years exposure
- Results:
  - Multiple regression analyses
  - Lung function decline most pronounced in sensitized subjects who continued to work in contact with lab animals
  - Average excess declines
    - FEV1 = 83 ml/y (p<0.05)
    - FVC = 148 ml/y (p<0.01)
    - MMEF = 7 ml/s/y (p=0.9)
- Results corroborate findings of other studies
  - Renstrom et al (Eur Respi J 1995)
- Proposed mechanism: Malo et al, *(J Allergy Clin Immunol* 1992) – chronic inflammation develops after sensitization, but before development of symptoms
- Low level inflammation leads to decline in lung function with continued exposure
- Study flaws- short follow up, ? Small sample size, unclear if workers “continually exposed” used PPE
General

- Trend illness data
  - 1°/ 2° LAA incidence
  - AHE & endotoxin co-exposure where no LAA sensitization
  - Prevalence
- Compare illness trend data to exposure (IH) data
- Re-evaluate Working OELs as needed
- Recent Stave and Darcey paper (May 2012)
Future Prevention?

- Immune modulation - increasing suppression of abnormal immune response?
- Summers, Elliott, & Weinstock- University of Iowa
  - *Trichuris suis* in Therapy of Inflammatory Bowel Disease
  - Theory: Hyper-reactive immune response may be diminished by intake of parasites
  - Stimulates suppressor arm of immune system
  - Study showed significant response of individuals with IBS to intake of Helminths
  - ? Possible application to other allergies such as LAA?
Implementation Actions Taken

- Used ‘surrogate’ exposure approach for AA / endotoxin exposures:
  - Focus on tasks involving exposures to rat / mouse allergens (i.e., RUP / MUP)
  - Endotoxin (primarily tasks involving feces exposures)

- Established “Working” OEL for:
  - Animal Allergens (i.e., RUP / MUP)
  - Endotoxin
  - Re-assess WOELs based on health outcome data

- Identified proper IH sampling & analytical methods
  - Animal Allergens – RUP / MUP
    - Simultaneous analysis only where simultaneous exposure potential
  - Endotoxin
    - Standardize methods & lab based

- QA/QC samples/ spike samples required per IHL protocol
Actions (cont’d)

- **Risk Management Control Strategy**
  - Where known “high risk” exposure potential, install engineering controls if not already present
    - Disposal of waste bedding
    - Washing cages
    - Box changing
    - Shaving fur
    - Changing of filters (HVAC/LEV systems)
  - Monitor exposures post control installation
  - Follow Control Banding Strategy for all other exposure potentials
    - Monitor employees’ exposures based on highest risk first + Health-related triggers
    - Investigate feasible engineering controls per FA Procedure

- **Use MRL Safety Network to leverage knowledge / information:**
  - IH Data –
    - Share task data & eliminate sampling where possible
  - Feasible Control Measures –
  - Incident Investigation Data, including any new cases
  - Lessons Learned
Actions (cont’d)

- Ensured all medical providers trained on:
  - Proper LAA classification (re: 1° & 2° LAA & injury / illness recordkeeping)
  - LAA incident investigation & notification protocol / requirements

- Evaluated suspected sensitization/LAA case
  - Notify GOH & investigate incident
  - Incident Investigation Team:
    - Site S&E
    - LAR
    - Site Health Service, Local Medical Provider
    - GOH as appropriate
Actions (cont’d)

- Trended illness data
  - 1°/ 2° LAA incidence
  - AHE & endotoxin co-exposure where no LAA sensitization
  - LAA prevalence

- Re-evaluating Working OELs based on health data and literature
  - Changed Endotoxin OEL
Recommended Working OELs

**Animal Allergens**
- Working OEL - Ceiling Limit = 5 ng/m³ (WOEL-C)
- No Wipe Limit established at this time
  - Used from a semi quantitative approach to evaluate transport of allergens / effectiveness of administrative controls

**Endotoxins**
- Working OEL-TWA = 90 EU/m³ (≈4.5ng/m³)
  - Incorporate “activity multiplier” (1-5X OEL-TWA based on duration of task) to address ‘peak’ exposure concerns
<table>
<thead>
<tr>
<th>Exposure Category</th>
<th>Airborne Concentration</th>
<th>Engineering Controls</th>
<th>Work Practice Controls</th>
<th>PPE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Low</strong></td>
<td>&lt; 5 ng/m³</td>
<td>No further controls required*</td>
<td>SOPs Maintenance Bedding, etc.</td>
<td>Per risk assessment</td>
</tr>
<tr>
<td><strong>Medium</strong></td>
<td>5 - 50 ng/m³</td>
<td>Feasibility Analysis required; Control at Source</td>
<td>“ “;</td>
<td>“ “; RPE required; if disposable, need QNTF</td>
</tr>
<tr>
<td><strong>High</strong></td>
<td>&gt; 50 ng/m³</td>
<td>Control at Source</td>
<td>“ “; Additional Admin</td>
<td>“ “; RPE with higher APF</td>
</tr>
</tbody>
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Merck Health Effects Estimates

Order of Magnitude (OOM) Estimates

- Prevalence Rate LAA$^1$ ~ 17%
- Estimated Incidence Rate$^2$ ~ <1%
- Estimated Total # LAA Cases - MRL$_{WW}$ ~ 351 existing cases (prevalence)
  - Does not include asymptomatic, but sensitized workers
  - Total exposed ~ 2066
- Projected Total # of New 1° LAA Cases (MRL) ~ 6/year
  - No additional action taken
- Projected # of New 2° LAA Cases ~ 39/year
  - 11% incident rate based on 100-person years (351 x 0.11)$^3$

$^1$OOM estimate based on current Rahway Prevalence Rate & Estimate of Impacted # of Workers (57/340)
$^2$OOM based on 2007 Rahway Incidence Rate data
$^3$Goodno L, et al. JOEM 2002: 44
Recommended Path Forward

- Communicate incident investigation protocol to site Health Services & Safety – GOH
  - Ensure proper illness investigation & recording

- Task Force – to define engineering controls / costs estimates for “High Exposure” tasks

- Leverage MRL Safety Network on findings / data/ controls (GSE – L. Schubert)

- Trend data
  - Injury / illness stats (GOH) & re-evaluate WOELs (GSE)
High Risk Tasks\textsuperscript{1}

- Disposal of waste bedding
- Changing of filters (HVAC/LEV systems)
- Washing cages
- Box changing
- Shaving fur
- Injections & other invasive procedures

\textsuperscript{1}Gordon S. et al, Occupat Medicine: 2003: 53
2011 LAA Trend Analysis

Laboratory Animal Allergy Trending

Year

Reported Number of Cases