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Occupational Exposure to Laboratory Animal Allergens

Sampling, Monitoring, and Analytical Methods

- White Paper -

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Introduction

Allergen exposure is a common cause of occupational asthma and other allergic diseases, particularly in vivaria and in laboratories that use animals on a regular basis. This had long been known to be a problem, but recent years have brought a significant increase in awareness of Laboratory Animal Allergens (LAA), combined with an increased regulatory and AAALAC inspection focus on exposure monitoring and worker protection.

Allergens are small proteins produced by a variety of sources, including dust mites, rodents, cockroaches, pollen, furry pets, molds, and foods. The allergens produced by mammalian LAA have multiple sources (i.e., hair, dander, urine, saliva, and serum). In a laboratory setting, rodent urinary allergens are predominantly hazardous as contaminants on inhaled airborne particulates, typically 0.5-10 microns in diameter. Laboratory workers become sensitized following prolonged exposure to airborne animal allergens, which are potent immunogens. Chronic exposure can cause wheezing and ultimately asthma symptoms. Direct contact of animals with the skin should also be avoided. Several studies have reported a high prevalence (20–40%) of sensitization in animal worker populations. Exposure response studies provide evidence that exposure to laboratory animal allergens may pose a considerable risk for sensitization even at very low exposure levels. (Bush 2001, Heederik et al 1999, Stave and Darcey 2012)

Engineering controls, personal protective equipment (PPE), and safety protocols can significantly reduce occupational allergen exposures. However, the implementation and performance evaluation of any allergen avoidance measures require reliable methods to quantify the actual exposures. This White Paper describes specific immunoassays used to evaluate animal allergen exposures, as well as airborne allergen sampling strategies using personal, task-oriented sampling; and exposure guidelines used in animal laboratory environments, to improve worker protection.

Laboratory Animal Allergens

The primary allergens of interest in animal facilities are proteins distributed to the environment via urine, dander, and/or saliva. In facilities with mice or rats, the main culprits are the urinary proteins and major allergens, **Mus m 1** and **Rat n 1**. Depending on the animal facility, other allergens may also be important, such as the major cat allergens **Fel d 1** and **Fel d 4**; dog allergen **Can f 1**, rabbit allergen **Ory c 3**, or guinea pig urinary proteins (**GPUP**).

While the individual proteins involved in laboratory animal allergy are diverse, all these allergens share certain common features: they tend to become airborne easily, and are readily soluble in aqueous environments, which aids exposure. They therefore represent a high risk for allergic sensitization and allergic disease in exposed individuals.

Industrial hygienists are frequently tasked with monitoring animal facilities to investigate specific complaints, establish risk assessment profiles, evaluate efficacy of engineering controls designed to limit exposure, monitor ongoing compliance with Occupational Exposure Limits (OEL), and monitor worker compliance with exposure control procedures. Ultimately, the aim is to prevent new sensitization of laboratory workers, and to reduce the risk of allergic symptoms in workers who are already sensitized to the animals.

LAA Sampling Procedures

Allergen exposure assessment in animal facilities is generally based on airborne allergen sampling of the work environment, or in the breathing zone of individual workers performing specific tasks. The sampling protocol most industrial hygienists follow involves using 25mm IOM samplers or 37mm cassettes (Figure 1) attached to a calibrated portable sampling pump, running at 2 Liters/minute. The sampling duration is dependent on the monitored task and goal, but typically ranges between 10 – 30 minutes. Personal sampling may be performed for a longer duration to determine a time-weighted average exposure. In this instance a minimum volume of 100 liters of air is collected, but may last an entire work shift. Area sampling may also be performed at higher flow rates to achieve a recommended target sample volume of 1,000 liters. Sampling media used in the sampling cassettes are usually glass fiber (GFA), polytetrafluoroethylene (PTFE), polyvinyl chloride (PVC), or mixed cellulose ester (MCE). Sampling pumps may need to be calibrated using a specific membrane material and pore size. Also, the sampling method may vary based on a specific situation and question.

Once sampling is completed, the cassettes are capped, packed in individual bags to protect from cross-contamination and condensation, and then shipped on ice to the analytical lab. If samples are not shipped within two days, samples should be stored frozen. In the laboratory, all air filter samples are extracted in PBS-T buffer (pH 7.4) for 2 hours at room temperature. The resulting extract is then used for allergen analysis using immunoassay methods. Sampling of settled dust, or surface wipe sampling may also be useful in specific situations. However, current OEL targets are based on airborne exposures.

Figure 1. 25mm IOM sampler and 37mm air sampling cassette

25mm Disposable IOM Cassette

3-piece 37mm Cassette

Allergen Detection using Immunoassays

Analysis of airborne allergens is performed using state-of-the-art immunoassay methods that utilize antibodies that specifically and sensitively recognize the allergen in question. For airborne allergen sampling, the immunoassay method of choice is the MARIA (Multiplex Array for Indoor Allergens). MARIA is a microbead-based method that allows the simultaneous detection of multiple analytes in a single test. Internally labeled microbeads are covalently coupled with allergen-specific antibodies, which capture the allergen in question to the bead surface. Following wash steps, a secondary, biotinylated allergen-specific antibody is added, followed by a streptavidin-coupled fluorophore. Results are generated using a Luminex/Bio-Plex instrument, which provides quantitative results for all bead types simultaneously. MARIA offers significantly improved sensitivity and reproducibility compared to the more traditional ELISA methods.

Assay Sensitivity and OEL targets

The current consensus OEL target applied by most industrial hygienists in pharma and biotech is 5 nanograms of allergen per cubic meter of air (**5ng/m^3**). The MARIA method enables exposure monitoring well below this OEL, even when using short-term sampling protocols (Table 1).

Table 1. Scenarios of Detection Limits based on Total Sampling Volumes

Sampling Duration	Sampling Volume (at 2 Liters/minute)	Lower Limit of Quantitation Mus m1	Lower Limit of Quantitation Rat n 1
10 min	20 Liters	1ng/m3	2ng/m3
30 min	60 Liters	0.33ng/m3	0.66ng/m3

Conclusions

- Occupational exposure to laboratory animal allergens puts workers at risk of sensitization and allergic disease.
- Reducing allergen exposure through procedures, engineering controls, and PPE should be a high priority.
- Implementing and monitoring exposure controls requires sensitive and specific methods for detection of airborne allergens.
- Airborne sampling combined with MARIA allergen detection allows health and safety managers and industrial hygienists to manage and improve occupational health and reduce worker allergic sensitization and morbidity.

References

1. RK Bush. 2001. Mechanism and epidemiology of laboratory animal allergy. ILAR J. 42:4-11.
2. Heederik D. et al. 1999. Exposure-response relationships for work-related sensitization in workers exposed to rat urinary allergens: results from a pooled study. J Allergy Clin Immunol. 103:678-84
3. Stave GM, Darcey DJ. 2012. Prevention of laboratory animal allergy in the US: a national survey. J Occup Environ Med. 54:55-63
4. King EM et al. 2013. A multi-center ring trial of allergen analysis using fluorescent multiplex array technology. J Immunol Methods. 387:89-95

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