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Research article

Airborne exposure to laboratory animal allergens

Howard J Mason * and Laura Willerton

Science Division, Health & Safety Executive, Harpur Hill, Buxton, SK179JN, United Kingdom

*** Correspondence:** Email: howard.mason@hsl.gsi.gov.uk; Tel: +44-129-821-8413; Fax: +44-129-821-8986.

Abstract: Exposure to laboratory animal allergens remains a significant cause of IgE-mediated occupational allergy and asthma. Since 2005, we have measured the major mouse and rat allergens (mus m 1 and rat n 1) collected on filters from air sampling in a range of UK and non-UK animal facilities. Supplied core data allowed us to construct an anonymized database of atmospheric results in ng m^{-3} containing 3080 mouse and 1392 rat analyses. Roughly twice as many static samples compared to personal samples had been sent for analysis. The medians (90^{th} percentiles) for the mouse and rat allergens employing personal atmospheric sampling were 2.6 (60.6) and 0.4 (12.4) ng m^{-3} respectively; for static samples the equivalent values were 0.2 (3.7) and 0.1 (1.4) ng m^{-3}. Where unequivocal sample descriptors were provided with samples, results were categorised to activities/areas. Medians and 90^{th} percentiles in these categories suggest that staff undertaking cleaning out, dumping of soiled bedding and cleaning cages can still have very substantial potential exposures in some facilities. The move to filtered cages appears to reduce general exposure, but filter changing and/or cleaning can lead to high exposures. In some facilities, animal receipt can cause significant exposures, as well as activities such as bleeding, culling and dosing; all activities involving the handling of animals outside of cages. We believe that the data presented may help those using air measurements in such facilities to improve their control of exposure to such aeroallergens, and thus reduce the risk of both sensitisation and subsequent allergic health problems, including the development of allergic asthma.

Keywords: allergens; mouse; rat; mus m 1; rat n 1; exposure monitoring

Abbreviations:

IVC	Individually ventilated cages
LAA	Laboratory animal allergens
LOD	Limit of detection

P90 Ninetieth percentile of the distribution of results

1. Introduction

The use of animals remains pivotal in many scientific and medical research studies undertaken in the pharmaceutical sector, contract toxicology laboratories, research institutes and universities. This is despite considerable activity to reduce their use and find alternative in-vitro, experimental models. In Great Britain some 3.8 million animals were used for scientific research in 2014 [1], mice accounted for 77% of all animals used with rats accounting for about another 7%.

Airborne exposure to LAA, especially from mice and rats, is well recognised as causing sensitisation and subsequent ocular, nasal, upper and lower respiratory symptoms [2,3]. However, life threatening anaphylaxis is uncommon and appears associated with rodent bites [4]. Besides provoking a range of symptoms in sensitised individuals, LAA are a proven [5] and major cause of occupational asthma. In 1999/2000 the annual UK incidence of asthma in those occupationally handling small animals was estimated as 1.56/1000 workers [6], although this incidence rate appears to have reduced since 2010 [7].

The sensitising agents in mice and rats are proteins found in the urine and saliva of the animals. This contaminates their fur and bedding and is readily aerosolised by activities of the animals or by technicians and scientists, who are looking after the animals or carrying out procedures on them. Potent major allergens [8], mus m 1 in mice and rat n 1, have been characterised, and a number of assays developed over the years that have been used to monitor atmospheric levels of these allergens. Initially such assays were based on competitive immunoassay using pooled sera from individuals sensitised to the allergens, latterly competitive, inhibition immunoassays based on animal antisera and non-competitive, sandwich immunoassays have been developed and reported. Sandwich immunoassays are considered the type of assay producing results with both adequate sensitivity and lack of bias. A European research study (Mocalex) suggested that competitive allergen immunoassays gave significantly higher results than non-competitive, sandwich assays [9,10]. Since 2005, HSL has undertaken mus m 1 and rat n 1 measurements on routine atmospheric monitoring samples collected in animal facilities using the same non-competitive sandwich immunoassay.

Health-based exposure limits are established on an understanding of the exposure-response relationship for the hazard in question. The understanding of such relationships for any allergen is very limited [11], being complicated by having at least two exposure-response relationships; one for initial sensitisation, identified by detection of serological specific IgEs or skin prick tests, and one (or possibly more) for the presentation of symptoms in those individuals already sensitised. The former relationship may be influenced by genetic susceptibility factors. The available publications specifically on LAA exposure-response relationships suggests that relationship for sensitisation are modified by atopy status [12], and will obviously be influenced by the common but variable use of respiratory protective equipment, if exposure is based on atmospheric levels of the allergens [13]. Studies have only found a relationship showing increased risk of sensitisation with length of exposure [14]. On an international basis, there appears to be no atmospheric exposure limits established for any protein allergen, except for the enzyme subtilisin [15]. Therefore in the absence of any defined exposure limit protecting against sensitisation and/or precipitation of symptoms, the control of exposure to as low as possible is paramount.

Given the importance of LAA in the overall cause of occupational asthma and the prevalence of allergic symptoms, we have reviewed the atmospheric mouse mus m 1 and rat n 1 monitoring data

undertaken at our laboratory. This is to help individual animal facilities interpret their own monitoring data, generally address the adequacy of their exposure control measures, identify higher risk activities or tasks and to help ensure exposure to allergens is as low as reasonably practical.

2. Materials and Method

Mus m 1 and rat n 1 allergens have been measured at HSE's Health and Safety Laboratory (HSL) using the same non-competitive enzyme-linked immunosorbent assay (Indoor Biotechnology, UK) in a microtitre plate format since 2005. These assays utilise a colorimetric amplification system that increases their sensitivity. The assays have been run on automated ELISA platforms, initially a Rosys Plato robotic system and then for the last six years using a Tecan Freedom EVO (Tecan, UK). Internal quality control samples are run immediately after standards and at the end of every microtitre plate. The quality control material is a dilution of mouse and rat urine in buffered solution containing 0.01% bovine serum albumin and is stored frozen. Quality control limit values for accepting results for each run have been established. The methods for both the mouse and rat allergen have been certified since 2010 by the United Kingdom Accreditation Service, ISO17025.

Samples are collected by a range of in-house and external occupational hygiene consultants and sent to HSL by courier, or first class post for UK samples. Our laboratory processes the filters, measures the extracted mus m 1 and rat n 1 allergens and reports back to the customer. The recommended sampling uses IOM (Institute of Occupational Medicine) samplers operated at flow rates of 2 L min^{-1}. Polytetrafluoroethylene (PTFE) filters (25 mm) are used in the cassettes, as initial work had shown that recoveries of mus m 1 and rat n 1 were higher and more reproducible than for glass fibre filters. Filters are extracted for 2 hours with mixing, using 2 ml of phosphate buffered saline buffer pH 7.4 containing 0.1% Tween 20 detergent. Recovery of mus m 1 and rat n 1 from PTFE filters had been shown in our laboratory to be 86% (CI 80–91%) and 79% (CI 75–84%) for mus m 1 and rat n 1 respectively. All results reported assume 100% recovery.

Although not obligatory, many of the submitters included the volume of air sampled, as well task/activity descriptors for individual samples. For results to be included in our analysis the minimum necessary amount of data was the nature of the sample (static or personal) and the air volume sampled. Often more information was supplied, such as the area sampled or the work task being undertaken. For those samples where unequivocal additional information about tasks or areas monitored was supplied, we have collated static samples and personal samples into a number of defined categories. We then looked to see if the data indicated some activities or areas in laboratory animal facilities with higher exposures, or where high 90^{th} percentiles (P90s) relative to the median levels may indicate significant differences across the sector in their control of exposure from specific tasks. All results were anonymised in terms of who submitted the samples, although where possible samples were identified as originating from the pharmaceutical industry, research institutes or universities.

The analytical limit of detection (LOD) for the mus m 1 and rat n 1 assays are 0.01 ng ml^{-1} and 0.02 ng ml^{-1} respectively, which equates to absolute amounts of allergen collected on filters of 0.04 ng of mus m 1 and 0.08 ng of rat n 1. This allows the calculation for each sample of a LOD in terms of ng m^{-3} based on the individual volume of air sampled. For those results less than the LOD, (LOD/✓2) was substituted and used in calculating the likely airborne exposure level in terms of ng m^{-3}. While calculated medians of airborne exposure levels reflect the better defined central tendency for defined populations and sub-populations, we consider that the P90 of exposure measurements can importantly indicate exposure levels where particular and immediate focus should be made to control exposure.

3. Results

The long-term, inter-assay coefficients of imprecision based on internal quality control samples are 14% and 21% for mus m 1 and rat n 1 respectively. These levels of imprecision have not significantly changed over the time frame of this report (2005–2016).

Three thousand and eighty results for mus m 1 and 1392 rat n 1 met the inclusion criteria for analysis in this study and this reflects around 63% and 53% respectively of the total number of mus m 1 and rat n 1 samples sent to HSL for analysis over this period. Of those meeting the inclusion criteria, 15% and 24% of mus m 1 and rat n 1 samples respectively were below the LOD. Thirty percent of the included measurements for mus m 1 and 39% for rat n 1 were personal atmospheric samples, the remainder were static air samples. Of the 82% of included results that could be assigned to one of the three broad sectors, 46% derived from the pharmaceutical sector, 21% from research institutes and 33% from universities.

Table 1 shows the cumulative overall medians and P90s by year of analysis. The cumulative P90 over time show little evidence of large fluctuations, being relatively stable with some suggestion of a decline for the cumulative mus m 1 P90 over time. As the number of included results increase over time, the confidence intervals (CI) have substantially decreased. The overall P90s of all mus m 1 and rat n 1 results up to the end of 2016 were 16.0 and 5.1 ng m^{-3} respectively. The distributions of results for both assays were not normally distributed and were skewed heavily to the right.

Table 1. Cumulative number of samples meeting the inclusion criteria, their cumulative medians and P90s with confidence intervals.

Time frame	mus m 1			rat n 1		
	n	Median	P90 (CI)	n	Median	P90 (CI)
2005–2007	196	0.24	57.0 (32.1–128.8)	258	0.11	9.7 (4.8–14.1)
2005–2008	442	0.31	43.5 (23.9–58.9)	454	0.08	4.8 (3.6–9.3)
2005–2009	591	0.46	30.2 (19.8–46.0)	548	0.09	5.5 (3.9–9.7)
2005–2010	757	0.34	21.8 (15.2–31.2)	652	0.08	4.2 (3.4 –6.5)
2005–2011	1086	0.35	19.7 (15.1–27.5)	829	0.09	4.8 (3.7–6.4)
2005–2012	1579	0.45	22.7 (16.2–28.9)	933	0.09	5.1 (4.1–7.2)
2005–2013	1984	0.44	23.9 (18.5–28.7)	1117	0.10	5.6 (4.4–7.0)
2005–2014	2462	0.41	18.3 (15.1–23.3)	1314	0.10	5.2 (4.2–6.5)
2005–2015	2653	0.41	18.5 (15.3–23.3)	1355	0.11	5.1 (4.2–6.3)
2005–2016	3080	0.41	16.0 (14.3–19.4)	1392	0.11	5.1 (4.2–6.3)

Table 2 and Figure 1 shows that measured atmospheric levels from static sampling were generally considerably lower than personal samples. This indicates that interpretation of air monitoring data needs to be undertaken separately for personal and static samples. The P90s 2005–2016 for mus m 1 are 60.6 and 3.7 ng m^{-3} for personal and static samples respectively; while for the rat allergen they are 12.4 and 1.4 ng m^{-3} for personal and static samples respectively.

Table 2. Medians and P90s (with their confidence limits) in ng m^{-3} for all samples and subdivided by type of sample.

	mus m 1		rat n 1	
Samples	Median	P90 (CI)	Median	P90 (CI)
All	0.4	16.0 (14.3–19.4)	0.1	5.1 (4.2–6.3)
Personal	2.6	60.6 (49.3–85.4)	0.4	12.4 (8.4–17.0)
Static	0.2	3.7 (3.1–4.7)	0.1	1.4 (1.0–2.3)

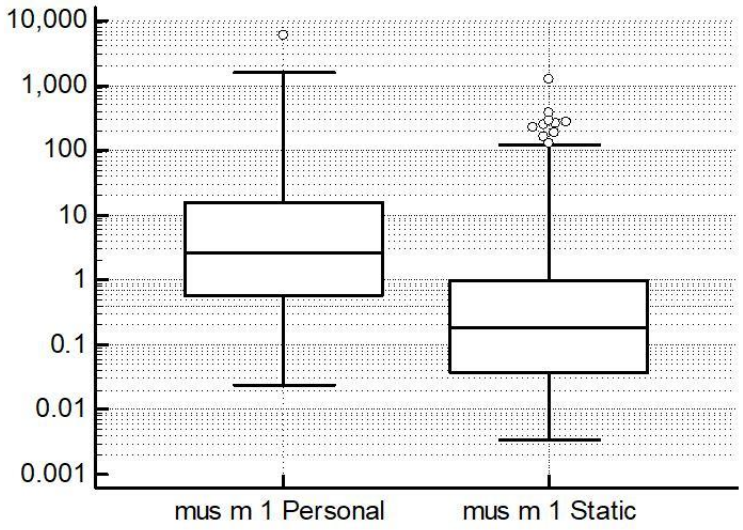

Figure 1. Box and whisker plot of mus m 1 air levels in ng m^{-3} categorised by type of sample.

Some 56% of the included samples could be aggregated into appropriate categories, although some have small numbers. Table 3 shows task-based monitoring by personal sampling and with any associated static sampling. Table 4 shows static monitoring data from various areas within laboratory animal facilities. Where 10 or more data points are available for aggregated data for activities and areas, a median and P90 in ng m^{-3} are shown. Albeit with small numbers for some categories, the P90s indicate that some high values can be identified with personal samples associated with animal receipt, dosing, bedding dumping, cage changing, cage scraping and washing, filter changing or cleaning and general cleaning (Table 3). Medians and P90 for holding rooms (Table 4) show the value of IVC cages over open caging in reducing the general atmospheric level of mouse allergen [16].

We have looked further to see if there is evidence of a decrease in the airborne levels over the time-frame of 2005–2016 (Table 5). For this we have used the mus m 1 data where there is a larger body of data and less derived results for LOD samples. For personal sampling, there does appear to be substantial decrease in the median and 90th percentile in the last 3 years of monitoring data (2014–2016). We have also looked at the percentages of mus m 1 in terms of being greater than the overall 2005–2016 defined P90s across the same time periods of data collection. This was to see if there is evidence that the defined overall P90 2005–2016 was highly influenced by earlier and possibly less controlled exposures. There was no obvious evidence of this influence.

Table 3. A breakdown of monitoring data in ng m^{-3} by various activities. These were taken from descriptors supplied with samples, and aggregated into the various specific activities. Aggregated activities with less than 10 participants are either not shown or shown as "-".

Task	Sample	mus m 1			rat n 1		
		N	Median	P90	N	Median	P90
Husbandry/animal care activity							
Unspecified activities	Personal	39	3.1	43.0	18	0.31	4.2
Animal receipt	Personal	10	10.0	72.6	26	0.63	8.4
Health checks	Personal	16	0.5	23.5	10	0.4	5.6
Using IVC cages	Personal	10	1.2	6.2	-	-	-
Experimental work activity							
Behavioural studies	Personal	10	1.85	15.2	-	-	-
Behavioural studies	Static	13	0.10	0.78	-	-	-
Bleeding	Personal	13	0.52	21.7	-	-	-
Culling	Personal	16	0.34	20.4	-	-	-
Dosing	Personal	15	4.3	101.0	10	1.9	6.1
Imaging	Static	10	0.3	4.3	-	-	-
Surgery/necropsy	Personal	32	0.23	8.9	30	0.21	1.6
Surgery/necropsy	Static	21	0.11	0.8	13	0.07	0.61
Removing soiled bedding from cages							
Bedding dump	Personal	26	35.9	129.1	38	5.5	26.5
Bedding dump	Static	39	2.9	87.8	20	0.5	12.4
Cage changing	Personal	33	28.2	432.2	27	5.8	40.4
Cage changing	Static	28	0.4	4.6	10	0.04	28.0
Cleaning and washing of cages after use							
Cage cleaning	Personal	31	5.5	59.2	13	4.9	23.6
Cage cleaning	Static	17	0.93	19.9	-	-	-
Cage scraping	Personal	16	102.2	204.9	-	-	-
Cage scraping	Static	12	2.9	57.6	-	-	-
Cage wash unspecified	Personal	59	6.8	109.1	24	1.2	31.7
Cage wash unspecified	Static	108	0.6	9.7	18	0.08	3.6
Cage wash 'dirty side'	Static	40	0.34	9.2	12	0.06	0.27
Cage wash 'clean side'	Static	24	0.04	1.7	10	0.03	0.1
Other activities in facilities							
Filter changing	Personal	23	1.0	107.5	11	0.7	7.9
Filter cleaning	Personal	12	48.5	247.0	10	2.8	33.2
General cleaning	Personal	24	0.47	104.8	12	2.1	7.5

Table 4. Breakdown of static monitoring data in ng m^{-3} by specific areas found within animal facilities. Results have been aggregated into the various appropriate areas from descriptors supplied with submitted samples. Aggregated area data with less than 10 samples are not shown, or shown as "-". Static samples where experimental activity took place are shown in Table 3.

Task	mus m 1			rat n 1		
	N	Median	P90	N	Median	P90
Monitoring rooms/areas where animals are kept and husbandry carried out						
Holding rooms, unspecified	133	0.3	7.3	66	0.08	4.3
Holding rooms, IVC cages	29	0.49	1.5	-	-	-
Holding rooms, open cages	10	9.6	25.9	-	-	-
Monitoring of other areas of facilities						
Corridor designated 'clean'	14	0.03	0.06	-	-	-
Corridor designated 'dirty'	20	0.05	0.89	-	-	-
Corridors/lifts, unspecified	192	0.06	1.7	100	0.07	0.35
Staff rest & tea rooms	44	0.04	0.16	17	0.06	0.09
Offices	86	0.04	0.18	54	0.06	0.21
Entrance lobby/reception	17	0.05	0.5	-	-	-
Changing rooms	82	0.07	0.5	22	0.07	0.28
Plant rooms	35	0.03	0.09	19	0.06	0.09
Laundry	28	0.04	0.07	-	-	-
Roof space	28	0.03	0.06	10	0.08	6.6
Other labs/spaces	30	0.19	1.9	12	0.08	1.9
Autoclave rooms	10	0.04	0.32	-	-	-

Table 5. Medians and P90s of airborne measurements for mus m 1 in ng m^{-3} subdivided into 3 yearly periods and by type of sampling.

Years	Personal samples			Static samples		
	N	P90	Median	N	P90	Median
2005–2007	66	85.2	2.7	88	4.78	0.05
2008–2010	190	48.9	4.3	343	3.00	0.05
2011–2013	324	95.2	5.5	868	5.56	0.25
2014–2016	311	28.1	1.3	745	3.01	0.20

4. Discussion

The value of any workplace monitoring measurement, whether environmental or biological, depends very largely on the availability of comparative data. Such comparative data could be formal workplace exposure limits (WELs) defined by regulatory or expert bodies, less formal data from benchmarking exercises in-house or monitoring data from workplaces carrying out similar activities. There has been historically a suggestion from within the pharmaceutical sector of "traffic light guidelines" for LAA exposure, where "green" is less than 5 ng m^{-3}, "amber" is 5–50 ng m^{-3} and "red" for exposures greater than 50 ng m^{-3}. More recently it has been suggested that exposures less than

5 ng m^{-3} are associated with a reduction or absence of LAA (personal communication). However, safe levels of exposure have still not been clearly defined or published, and dose-response relationships may be complicated by significant individual susceptibility factors, such as atopy status and existing sensitisation to other small furry animals [17,18]. Therefore we believe it is helpful to share an analysis of our airborne exposure data collected from a wide range of LAA facilities in order to help individual facilities interpret their monitoring results against peer group data.

The data emphasise the differences in exposure identified using personal air sampling, i.e. with the sampler located in the breathing zone of a worker and a static background measurement collecting dust samples within a specific area where specific tasks may be carried out. The data reinforces that proximity to the allergen source, whether directly from the animal itself or contaminated bedding and cages, substantially increases potential or actual exposure, depending on the nature of any RPE used. Interestingly, those sending samples for measurement to our laboratory appear to favour collecting static samples over personal monitoring by a factor of almost 2:1. Whether this is due to operational reasons or greater ease in taking static samples is unclear, however an over-reliance on collecting static air samples may under-estimate potential exposure to staff.

The data in Table 5 for mus m 1 personal samples suggest a reduction in median and P90 for the last 3 years of data in comparison with the previous years. This is not reflected in the static monitoring data. It is impossible to prove with complete certainty that this reflects a real improvement in exposure control rather than bias in samples. However, we would point out that since November 2014 we have included cumulative P90 values within the interpretation section of the report we return to our customers. Also the value of the P90 approach in terms of driving down occupational exposure over time, especially if the P90 is reviewed at intervals, has been shown in the field of biological monitoring [19].

Without a full understanding of the dose-response concerning both processes of initial sensitisation to allergen and precipitation of symptoms in those already sensitised, monitoring data may still help reduce the risk from the highest exposures as well as generally reduce overall exposure in this sector. A few studies have suggested that there is no clear relationship between measured atmospheric levels and the risk of sensitisation and symptoms, only with the duration of exposure [14]. This lack of a clear health risk relationship with atmospheric levels may be due to a number of reasons. The inappropriate nature of the collected exposure data and study design, the influence of atopy status on the risk of sensitisation, the biological role of mus m 1 in causing sensitisation and other co-exposures such as endotoxin [20], and whether RPE is worn, may obscure a real relationship. We believe that an ongoing focus on reducing exposure, particularly where high levels are encountered, remains a key driver to protect the health of animal laboratory workers [8].

Driving down the measured atmospheric exposure over time will only occur through improvements to engineering or technical control measures, simply putting staff in RPE with higher protective factors will not influence it. Given the well-known issues with the proper use of RPE and its position within the hierarchy of control measures, it is appropriate for the focus to be on better engineering and technical control of exposure.

A number of activities/tasks have been historically considered as associated with high potential exposures, without necessarily a large body of published data to confirm this. These activities include cage cleaning, changing bedding and getting rid of soiled bedding [21,22]. Automated cage washing and equipment to facilitate bedding dumping, albeit expensive, has been introduced in some laboratory animal facilities, especially within the pharmaceutical sector. The calculated P90s for task-based personal monitoring suggests that in some facilities individuals may still have potentially very high exposures carrying out these activities. For example, our median values for mus m 1

personal sampling for bedding dumping, cage changing and cage scraping are close to, or breach the overall P90 of 60 ng m^{-3} (Table 2). This suggests around 50% of results for these tasks are close to or over this value. The data, albeit limited to mus m 1, suggests any activity considered as 'cage scraping' needs to be eliminated or be carried out under very stringent control. Overall for those processing or removing soiled bedding or cleaning used cages, the data suggest that in many of the monitored facilities there is the need for the use of high levels of respiratory protective equipment, if appropriate engineering controls cannot be implemented.

Other recent changes include the general move to filtered or IVCs for housing laboratory rodents [21]. Unfortunately descriptors for our submitted samples have not always indicated the specific nature of the caging used. However, in our husbandry associated data there is limited evidence that confirms the use of IVCs are associated with a reduction but not elimination of atmospheric mus m 1 in comparison with open cages [23]. Many facilities also have sophisticated air management systems. However with any ventilation and filtration system, maintenance of filter cleaning or changing has often been identified with high exposures across a number of sectors. Indeed our data suggests that filter changing, but particularly filter cleaning, can be associated with the generation of potentially high allergen exposures and may need special attention to protect staff undertaking such activities. There was also evidence of high levels of mus m 1 for general cleaning in a limited number of facilities. From the data in this study it is not possible to identify which general cleaning tasks, or how they were undertaken, may lead to high allergen exposures. Those responsible for health and safety in such facilities may need to ensure good practice to ensure aerosols of allergen are not regenerated from any dust reservoirs during cleaning tasks.

Some husbandry activities can be associated with high exposures. There was evidence to suggest that 'animal receipt', which will include animal handling, can be associated with higher exposure levels, as well as in some facilities related to general husbandry tasks. Experimental tasks are invariably associated with some degree of animal handling outside of the caging. Based on limited data "dosing" is an activity that can lead to high personal exposures in some facilities. Culling, bleeding and surgical procedures (invariably necropsy, post-mortem tissue harvesting) appear to be associated with lower personal exposure than dosing. The use of ventilated tables to reduce allergen exposure from animal handling has been recommended [22].

This study utilises data from unselected workplaces handling mice and rats and therefore there is significant potential for biases to be introduced in extrapolating from our database to the wider sector. However, significant numbers of samples have come from universities and research institutes, as well from the pharmaceutical sector both in the UK and internationally. We believe that the large number of samples in our database from over 100 different sites may mitigate this potential weakness. A significant minority of measurements was below the limit of detection for respective assays and we used a mathematical formula to include such results. For the mice measurements, the number of these derived results is unlikely to have introduced uncertainty in the derived overall P90 or even the median values.

We hope the data in this paper will help those responsible for health and safety in LAA facilities, in terms of the overall value of monitoring, the targeting of any monitoring and acting on the results to prevent the risk of sensitisation and symptoms in staff. It is our intention to continue adding to this cumulative database of LAA monitoring results and produce reviews of the data and reassigning the P90 levels at appropriate intervals.

5. Conclusions

Those responsible for protecting their workforce in laboratory animal facilities need to comply with their appropriate regulatory authority's legislation or guidance. However, we believe that the following is a logical approach to using atmospheric monitoring data within an exposure control strategy. Tasks and activities where there remains high exposures in some facilities are identified in this paper; these can be subjected to close scrutiny. Any measured airborne level over the appropriate, current P90 (e.g. >60 ng m^{-3} for mus m 1 in personal samples) needs to lead to immediate action to reduce and control such exposures. For levels over the approximate median value but less than the P90 (e.g. 3–60 ng m^{-3} for mus m 1 in personal samples), the control measures in place should be reviewed with the definite aim of reducing exposure. For levels less than the median value (e.g. <3 ng m^{-3} for mus m 1 in personal samples), those responsible should not assume that such workers or tasks are safe but continue an ongoing process to ensure that all exposures are kept as low as practicable.

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Conflict of Interest

Both authors are involved in research concerning occupational allergen exposure and operating a commercial aeroallergen monitoring service at HSE's Health and Safety Laboratory. All authors declare that they have no conflict of interest in this paper.

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