Project Title and NPB project identification number
Determine the respiratory health risks associated with swine production using the QMRA approach, NPB project #21-090

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1. Industry Summary:

The objective of the project is to determine the occupational and community health outcomes associated with swine production with an emphasis on respiratory health outcomes, using a standard quantitative microbial risk assessment (QMRA) approach. The outcome is an evaluation of the respiratory health risks, based on an understanding of the hazards and hazardous events in swine production, and validity of control measures and their relative significance. It aims to provide science based evidences to determine if the health hazards are adequately controlled, to identify the risks that are critical for the respiratory health outcomes, and to help to select the best steps to reduce these risks. The purpose is to inform operation and management on necessary improvements and upgrades to reduce the risks, and to help swine producers focus on the most needed improvements. Swine production generally involves a substantial amount of waste materials on-site that contain various pathogens. Dust in swine barns consists up to 90% organic matter and is often biologically active. Exposure to pathogenic dust is a health issue for workers inside swine barns and a potential health concern for people residing adjacent to swine facilities. Endotoxin, a building stone of the outer membrane of Gram-negative bacteria, is associated with swine dust, and considered as the most important respiratory hazards that affect the health and welfare of swine farmers and their neighbors. An exhaustive literature search and a systematic review were conducted to collect all the scientific data related to respiratory health risks associated with swine production. The levels of endotoxin exposure were generally proportional to the levels of inhalable particulate matter (PM) in swine farms. The majority of endotoxin are associated with inhalable PM instead of respirable PM. This is reasonable since the main endotoxin sources are dust particles from feed, manure, and animals, which are generally larger than the size range of respirable PM. When endotoxin measurements are not available, the concentration of endotoxin in swine facilities can be estimated by multiplying the concentration of inhalable PM with the estimated endotoxin level per mg of inhalable PM. On average, there were around 900 endotoxin units (EU) per mg of inhalable PM in swine facilities. During feeding activities or in finishing facilities, the endotoxin levels increase to around 1800 EU per mg of inhalable PM. The No-Observed-Effect-Level (NOEL) of endotoxin exposure was estimated to be 595 EU/m^3 based on all the available data in the literature. The changes of FEV_1, which represents the amount of air that can be exhaled forcibly within one second, was used to determine the dose-response relationship for endotoxin exposure. The endotoxin exposure in swine facilities ranged from 400 to 6500 EU/m^3. Much of the reported concentrations in swine facilities exceeded the estimated NOEL. At the typical exposure level, various respiratory symptoms may be observed, but the resulting FEV_1 decreases are mostly less than 20%, which is still considered as normal; the chance of resulting ΔFEV_1>20% is much lower than 2.5%. Higher endotoxin levels were observed during feeding activities, and in finishing facilities. Especially, activities such as power washing and hog load-out could generate high endotoxin exposure that result in ΔFEV_1>20% for smokers. Smokers were generally more sensitive to endotoxin exposure than non-smokers. Although the daily occupational and community risk of reduced lung function is generally low, the accumulated long term risk could be significant. Given the estimation of 900 EU endotoxin per mg of inhalable PM, when the inhalable PM concentration is larger than 0.7 mg/m^3, it is likely that the associated endotoxin concentration will be larger than the 595 EU/m^3 NOEL. Since the majority of

endotoxin are associated with inhalable PM, any mitigation strategies that can reduce inhalable PM will contribute to the reduction of associated endotoxin concentration, which may include increasing fat content in feed, wet feeding, automated dry feeding, full concrete floor, oil spraying, ventilation, use of personal protection equipment, etc.

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2. Key Findings:

- The No-Observed-Effect-Level (NOEL) of endotoxin exposure was estimated to be 595 EU/m^3.
- Endotoxin exposure in swine facilities ranged from 400 to 6500 EU/m^3. Much of the reported concentrations in swine facilities exceeded the estimated NOEL. At the typical exposure level, various respiratory symptoms may be observed, but the resulting FEV_1 decreases are mostly less than 20%, which is still considered as normal.
- The majority of endotoxin are associated with inhalable PM instead of respirable PM. On average, there were around 900 EU endotoxin per mg of inhalable PM in swine facilities. During feeding activities or in finishing facilities, the endotoxin levels increase to around 1800 EU per mg of inhalable PM.
- Higher endotoxin levels were observed from task-based measurements during feeding activities, and in finishing facilities. Especially, power washing and hog load-out could generate high endotoxin exposure that result in ΔFEV_1>20% for smokers.
- Smokers were generally more sensitive to endotoxin exposure than non-smokers, and involve more uncertainties.
- The non-kinetic test methods could significantly underestimate the endotoxin level.
- Although the daily occupational and community risk of reduced lung function is generally low, the accumulated long term risk could be significant.

3. Keywords:

Swine, endotoxin, inhalable PM, respiratory hazards, lung function, occupational health, risk assessment.

4. Scientific Abstract:

Dust in swine barns consists up to 90% organic matter and is often biologically active. Exposure to pathogenic dust is a health issue for swine workers and nearby community. Endotoxin is considered as the most important respiratory hazards that affect the health and welfare of swine farmers and their neighbors. The objective of the project is to determine the occupational and community health outcomes associated with swine production with an emphasis on respiratory health outcomes, using a standard quantitative microbial risk assessment (QMRA) approach. The framework for QMRA of swine production is a standard four-step process, which includes: 1) problem formulation, 2) exposure assessment, 3) health effects assessment, and 4) risk characterization. An exhaustive literature search and a systematic review

were conducted to collect all the scientific data related to respiratory health risks associated with swine production. Meta-analysis was conducted to generate all the quantitative input needed at each step. The levels of endotoxin exposure were generally proportional to the levels of inhalable PM in swine farms. The majority of endotoxin are associated with inhalable PM instead of respirable PM. On average, there were around 900 endotoxin units (EU) per mg of inhalable PM in swine facilities. During feeding activities or in finishing facilities, the endotoxin levels increase to around 1800 EU per mg of inhalable PM. The No-Observed-Effect-Level (NOEL) of endotoxin exposure was estimated to be 595 EU/m^3. The changes of FEV_1, which represents the amount of air that can be exhaled forcibly within one second, was used to determine the dose-response relationship for endotoxin exposure. The endotoxin exposure in swine facilities ranged from 400 to 6500 EU/m^3. Much of the reported concentrations in swine facilities exceeded the estimated NOEL. At the typical exposure level for swine workers, various respiratory symptoms may be observed, but the resulting FEV_1 decreases are mostly less than 20%, which is still considered as normal; the chance of resulting ΔFEV_1>20%, which represents an obstruction in lung function, is much lower than 2.5%; and the 95% confidence interval of FEV_1 decrease was from 3.9% to 6.7% for non-smokers. Higher endotoxin levels were observed from task-based measurements during feeding activities, and in finishing facilities. Especially, activities such as power washing and hog load-out could generate high endotoxin exposure that result in ΔFEV_1>20% for smokers. Smokers were generally more sensitive to endotoxin exposure than non-smokers, and involve more uncertainties. Although the daily occupational and community risk of reduced lung function is generally low, the accumulated long term risk could be significant. At an estimated daily risk of 0.04%, the long term risks of experiencing one or more respiratory symptoms are estimated to be 13% for 1 year, 24% for two years, 34% for 3 years, 43% for 4 years, 50% for 5 years, and 57% for 6 years.

5. Introduction:

Swine production generally involves a substantial amount of waste materials on-site that contain various pathogens. Exposure to pathogenic dust is a health issue for workers inside swine barns and a potential health concern for people residing adjacent to swine facilities (Basinas et al., 2015). A variety of contaminants, microbial agents, and health effects associated with swine production have been documented in both occupational and community studies (Cole et al., 2000). Increased risks for bronchitis, COPD (Chronic obstructive pulmonary disease), and reduced FEV_1 (forced expiratory volume in one second) have been reported in swine farmers (Omland, 2002; Eduard et al., 2009).

Exposure to pathogenic dust can take place through inhalation, skin contact, or through the gastrointestinal system. Dust in swine barns consists up to 90% organic matter (Aarnink et al., 1999) and is often biologically active. It can adsorb and contain a great number of substances including pathogenic micro-organisms and bioactive components such as endotoxins, antibiotics, allergens, dust mites, and beta-glucans; irritating gases such as ammonia; odorous compounds; and heavy metals (Donham et al., 1986; Cambra-Lopez et al., 2010). Attached to fine dust, these components could increase the potential health hazard of dust if they have access to the deeper respiratory airways, enhancing the biological effect of dust (Donham and Leininger, 1984). Inhaled dust particles can penetrate in the deeper respiratory airways, compromising animal's and human's respiratory health, contributing to increased occurrence of chronic cough and/or phlegm, chronic bronchitis, allergic reactions and asthma-like symptoms amongst swine farmers (Donham, 1990; Radon et al., 2001b).

Endotoxin, a building stone of the outer membrane of Gram-negative bacteria, is considered a main cause of respiratory disease among farmers because of its extreme potency in comparison with other pro-inflammatory microbial constituents of bioaerosols (Basinas et al., 2015). Endotoxin-contaminated bioaerosols are considered as the most important respiratory hazards that affect the health and welfare of swine farmers and their neighbors (Reynolds et al., 1996; Vogelzang et al., 1998; Cambra-Lopez et al., 2010).

As swine operations are becoming larger and more intensive, public concerns on community health are growing. Moreover, because many operations now have more than 10 employees, occupational health of workers has become more relevant (Donham, 2010). A significant component of the pork industry has differentiated from traditional family farming and has developed like other industries in management, structure, and concentration. Exposure control and prevention strategies for swine farmers are urgently required (Basinas et al., 2015). However, our ability to define and quantify the occupational and community health risks associated with swine production is still limited.

Quantitative microbial risk assessment (QMRA) is a standard risk assessment framework that allows for quantitative scientific data to be interpreted in the context of estimated health risks associated with a system, e.g., the swine production system. QMRA combines scientific knowledge about the presence and nature of pathogens, their potential fate and transport in the environment, the routes of exposure of humans and the health effects that may result from this exposure, as well as the effect of natural and engineered barriers and hygiene measures. It is a systematic way to combine all the existing knowledge into a single assessment that allows evidence-based, proportionate, transparent and coherent management of the health risks (WHO, 2016).

The process of QMRA includes a systematic evaluation of: 1) Hazards – specifically, the pathogens that may have an adverse impact on human health; 2) Hazardous events – events that may introduce pathogens into the environment; and 3) The adequacy of the controls to reduce the risks – control measures that could be used to reduce these hazards to an acceptable level, including engineered controls such as mitigation process, and non-engineered measures such as hygiene protocols for workers.

The outcome of QMRA is an evaluation of the health risks associated with the system, based on an understanding of the hazards, hazardous events, and validity of control measures and their relative significance. The results may show that the current system is safe and provide the justification for this conclusion, or it may highlight shortcomings in the current system design, operation or maintenance, and support the prioritization of these shortcomings according to their health risk and thus the priority for management. The numerical output of QMRA can address the risk management questions in finer detail and allows for more precise comparison between different risk management options.

As many researches have been published on occupational and community health concerns associated with swine production (Cole et al., 2000; Donham, 2010; Basinas et al., 2015), the available data in literature have provided an opportunity for conducting a comprehensive QMRA on the health risks associated with swine production.

6. Objectives:

The objective of the project is to determine the occupational and community health outcomes associated with swine production with an emphasis on respiratory health outcomes, using a standard QMRA approach. The outcome of QMRA is an evaluation of the respiratory health risks, based on an understanding of the hazards and hazardous events in swine production, and validity of control measures and their relative significance. It aims to provide science-based evidences to determine if the health hazards are adequately controlled, to identify the risks that are critical for the respiratory health outcomes, and to help to select the best steps to reduce these risks. The purpose is to inform operation and management on necessary improvements and upgrades to reduce the risks, and to help swine producers focus on the most needed improvements.

The framework for QMRA of swine production is a standard four-step process, which includes: 1) problem formulation, 2) exposure assessment, 3) health effects assessment, and 4) risk characterization. Each component of the assessment was explicitly quantified.

An exhaustive literature search and a systematic review were conducted to collect all the scientific data related to respiratory health risks associated with swine production. The literature search included journal papers, government report, popular press magazines, Quarterly Hogs and Pigs reports, Pork Information Gateway, etc. Meta-analysis was conducted to generate all the quantitative input needed at each step for the QMRA, e.g., endotoxin concentrations in the air, infectivity of the pathogens, exposure time, bioaerosol ingestion rate, etc. Meta-analysis is a quantitative statistical analysis of a collection of results from individual previous studies for the purpose of integrating the findings. Results from meta-analyses are usually more robust and have less bias than individual studies because of improved statistical power.

7. Materials & Methods:

7.1 Problem formulation

The scope and overall context (hazard identification, exposure pathways, and health outcomes of interest) of the QMRA were carefully defined in order to bring fundamental knowledge and application for continuous improvement relating to environmental stewardship in the pork industry.

First, hazard identification is predominantly a qualitative process intended to identify pathogens of concern. Early occupational studies have focused on gases and non-biologic aerosols in swine barns because their health effects and occupational exposure limits were generally well documented. However, bioaerosols, particularly endotoxins, have emerged as important agents in causing adverse respiratory health effects (Cole et al., 2000), and was a focus of this study. Second, the overall exposure pathway was identified systematically from source to exposure, including pathogen sources, environmental fate and transport barriers, environmental or engineered barriers, and human activities that may lead to different levels of exposure. Last, the human health outcomes were identified from literature review of epidemiologic studies that documented symptoms in workers, as well as mechanistic studies that exposed human volunteers to endotoxins in laboratory.

7.2 Exposure assessment

Relying on the scope defined during problem formulation, the exposure assessment was undertaken to quantify the magnitude and frequency of exposure to inhalable PM and endotoxin via the identified exposure pathways and hazardous events in swine production.

The exposure pathway for occupational exposure will be defined in terms of pathogen sources (the point of initial pathogen quantification), engineered or regulatory control measures/barriers, and mechanisms of exposure, generally as a set of exposure scenarios. Each component of the exposure pathway was quantified based on the best available scientific data in literature, and an understanding of the expected variability and uncertainty associated with the model variables. Quantitative information was compiled on the endotoxin concentrations in swine houses and fate of endotoxin during normal and incident situations. Airborne endotoxin concentrations were in the unit of ng m^{-3} or μg m^{-3} for some studies before 2000. Quantified units of endotoxin were converted in order to be comparable with the units used in the following dose-response assessment (1 ng endotoxin = 10 endotoxin units (EU), Thorne et al. 1997 & Schwartz et al. 1995).

7.3 Health effects assessment

The most reliable way to measure changes in lung function is by using FEV_1, which represents the amount of air that can be exhaled forcibly within one second. The No-Observed-Effect-Level (NOEL) was calculated as the endotoxin concentration at which average FEV_1 changes were zero, through regression using all the available data in the literature.

Endotoxin doses for swine workers were calculated using the equation: Endotoxin dose = inhalable endotoxin concentration × exposure time × inhalation rate. Dose-response relationship describing the relationship between exposure and the degree of FEV_1 decrease was determined for endotoxin through meta-analysis. A FEV_1 decrease larger than 20% represents an obstruction in lung function. The beta-Poisson dose-response function (Mara et al., 2007; Eisenberg et al., 2008; Brooks et al., 2012) and the logarithmic dose-response function (Rylander et al., 1985; Castellan et al., 1987) were compared, and the logarithmic dose-response function was selected due to better performance. Based on the dose-response curve, the 95% confidence interval of FEV_1 decreases were determined for endotoxin dose under various situation.

7.4 Risk characterization

The information from the exposure assessment and the health effects assessment were combined to generate a quantitative measure of risk for the defined conditions and scenarios. A long term individual-level risk is defined as the risk associated with an individual's exposure over a long period. It is calculated from the daily individual-level risk as:

$$\text{Long term risk} = 1-(1-P)^t$$

in which, P is the daily individual-level risk and t is the time exposed in days.

8. Results:

8.1 The overall exposure pathway

Exposure levels are highly variable at different locations in swine farm and are associated with activities such as feeding. The exposure levels increase markedly during feeding time. Highest exposure was observed for workers in finishing stables (Louhelainen et al., 1987; Chang et al., 2001) or workers in weaning stables (Mc Donnell et al., 2008). Lowest exposure was observed in dry sows, or in breeding and farrowing units (Chang et al., 2001; Mc Donnell et al., 2008). Exposure levels were higher during feeding tasks, especially in farmers that used floor feeding methods, feed with high moisture or indoor grinding (Holness et al., 1987; Larsson et al., 1992). Increased fat content in feed associated with decreased dust exposure (Vinzents & Nielsen, 1992). Controlling, cleaning and tasks involving active animals (e.g., castration, teeth cutting, piglet weaning) also increased exposure (Preller et al., 1995; O'Shaughnessy et al., 2010). The most highly associated tasks with endotoxin exposure included ear tagging, teeth cutting, and floor sweeping (Basinas et al., 2015).

Exposure to pathogenic dust can take place through respiration, inhalation, skin contact, or through the gastrointestinal system. A diagram was constructed to illustrate all system components that need to be evaluated in the risk assessment of swine production system (Figure 1).

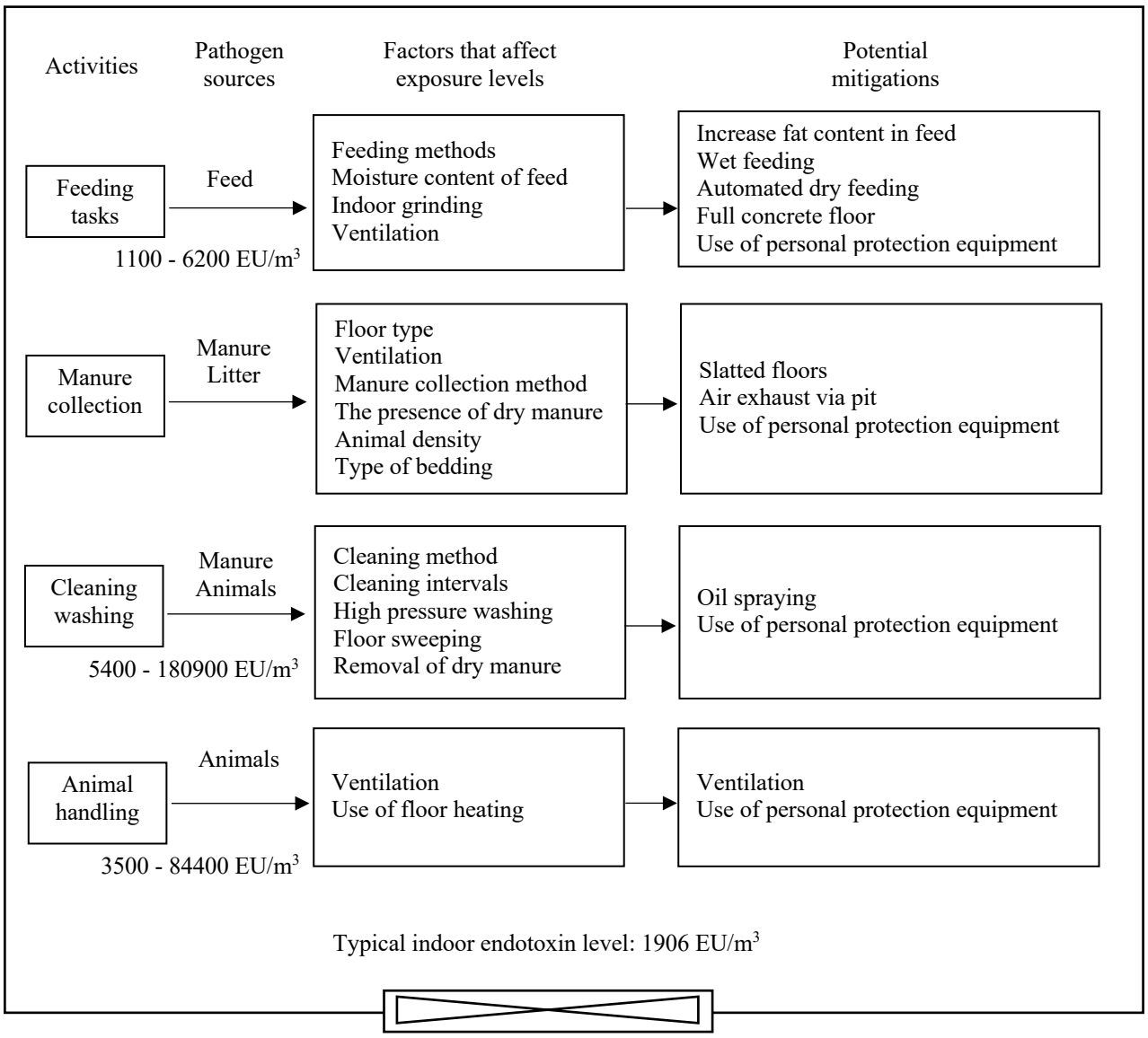

Figure 1. The overall endotoxin exposure pathway in swine production

8.2 Exposure assessment

The exposure levels of dust and endotoxins in swine barns are highly variable, and, in most cases, exceed by several folds up to orders of magnitude the established occupational exposure limits (OEL). In most cases, the temporal (day to day) within-workers variations is much larger than the between-workers variations (the variations in average concentrations among workers). Feeding practices, the type of ventilation, type of floor, and the outdoor temperature remained strong determinants of endotoxin exposure levels. Exposure data from task-based measurements in the literature are listed in Appendix 1. Exposure data from stationary sampling measurements in the literature are listed in Appendix 2.

Effect of measurement methods

Various methods have been used to measure endotoxin. The most widespread endotoxin test is the limulus amebocyte lysate (LAL) test, introduce in 1970s. LAL is an aqueous extract of horseshoe crab blood cells (amoebocytes). The LAL reagent reacts with bacterial endotoxin and lipopolysaccharide (LPS), a component of Gram-negative bacteria's membrane. This reaction serves as the foundation for the LAL reagent, which is used to detect and quantify bacterial endotoxins (Mehmood, 2019). The LAL test methods can further be classified as the gel-clot end-point methods and the kinetic methods (chromogenic or turbidimetric testing). Kinetic methods have great sensitivity as 0.001 EU/ml of lysate, while the sensitivity of non-kinetic methods is only 0.015 EU/ ml (Tim, 2016).

The levels of endotoxin exposure were generally proportional to the levels of inhalable PM in swine farms. However, the endotoxin levels measured by the kinetic methods were much higher than that measured by the non-kinetic methods. Figure 2 showed the relationship between endotoxin and inhalable PM for all the endotoxin data measured using the kinetic methods, including both task-based measurements and stationary sampling measurements. When using the kinetic methods, on average, around 900 EU endotoxin were detected per mg of inhalable PM. As a comparison, when using non-kinetic methods, only around 50 EU endotoxin were detected per mg of inhalable PM. The non-kinetic methods could have significantly underestimated the endotoxin level. Therefore, only the endotoxin data measured using the kinetic methods were used in the following analysis.

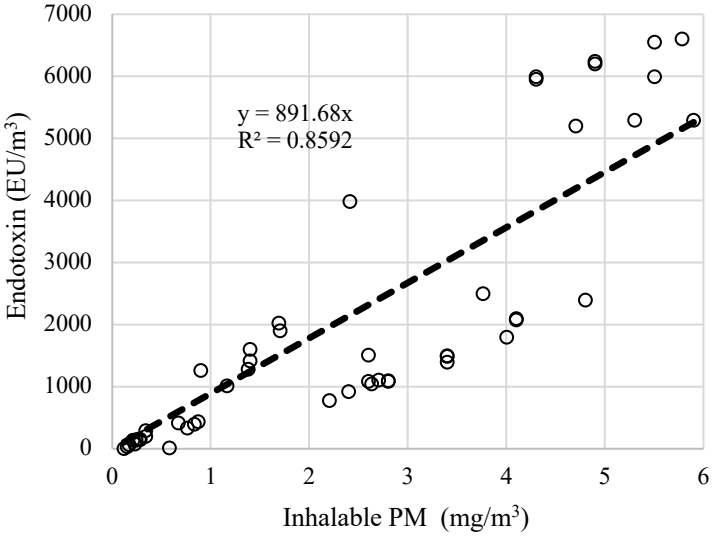

Figure 2. Concentrations of endotoxin vs. inhalable PM for all the endotoxin data measured using the kinetic methods in swine farms

Task-based measurements vs. stationary sampling measurements

The concentrations of inhalable PM and associated endotoxin from task-based measurements were generally larger than that from stationary sampling measurements (1 to 6 mg/m^3 PM and 400 to 6500 EU/m^3 for task-based measurements vs. 0.1 to 0.9 mg/m^3 PM and 9 to 1300 EU/m^3 for stationary sampling measurements). The concentrations of respirable PM and associated endotoxin from task-based measurements were in the similar range with that from stationary sampling measurements (0.2 to 0.5 mg/m^3 PM and 6 to 70 EU/m^3 for task-based

measurements vs. 0.1 to 0.7 mg/m^3 PM and 10 to 130 EU/m^3 for stationary sampling measurements). On average, in the task-based measurements, the concentrations of inhalable PM were about 20 times higher than that of respirable PM, while in the stationary sampling measurements, the concentrations of inhalable PM were only about 38% higher than that of respirable PM.

The ratios of the endotoxin concentrations over the concentrations of inhalable PM were similar (around 900 EU/mg) for the task-based measurements and the stationary sampling measurements.

Endotoxin in inhalable PM vs. endotoxin in respirable PM

As seen in Figure 2, on average, around 900 EU endotoxin were detected per mg of inhalable PM based on data from both task-based measurements and stationary sampling measurements. The endotoxin level in respirable PM was much less comparing with that in inhalable PM. As seen in Figure 3, on average, around 500 EU endotoxin were detected per mg of respirable PM. On average, in the task-based measurements, the concentrations of endotoxin in inhalable PM were about 36 times higher than that of respirable PM (400 to 6500 EU/m^3 in inhalable PM vs. 10 to 130 EU/m^3 in respirable PM).

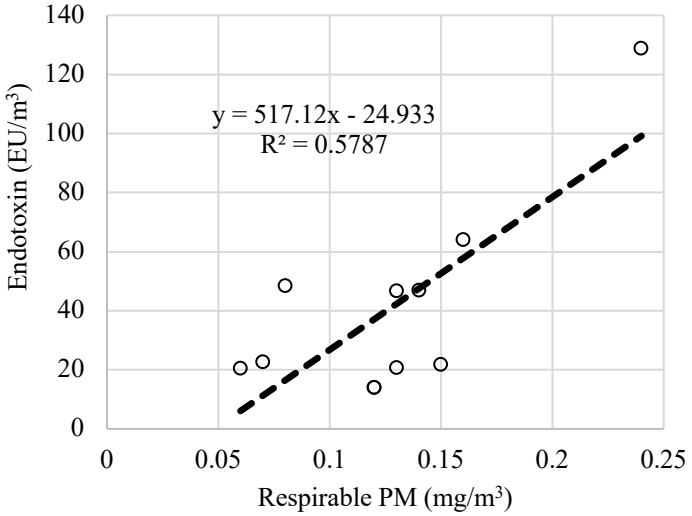

Figure 3. Concentrations of endotoxin vs. respirable PM

Endotoxin during feeding activities

Higher endotoxin levels were observed from task-based measurements during feeding activities. During feeding activities, not only the concentrations of inhalable PM were higher, the endotoxin levels per mg of inhalable PM were also higher than normal. Around 1800 EU endotoxin were detected per mg of inhalable PM during feeding activities (Figure 4), which was twice higher than the normal level (900 EU/mg of inhalable PM).

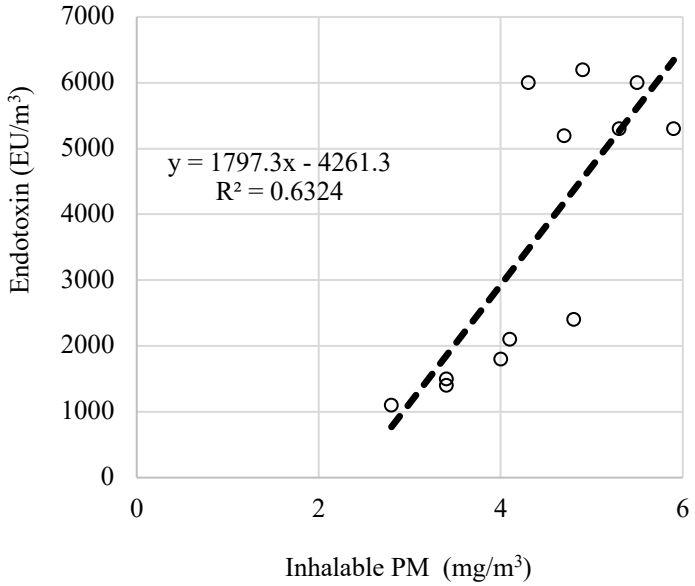

Figure 4. Concentrations of endotoxin vs. inhalable PM during feeding activities

Endotoxin in finishing facilities

Higher endotoxin levels were observed from both task-based measurements and stationary sampling measurements in finishing facilities. In finishing facilities, the concentrations of inhalable PM were similar (ranged from 1 to 4 mg/m^3), but the endotoxin levels per mg of inhalable PM were higher than other types of facilities. Around 1800 EU endotoxin were detected per mg of inhalable PM in finishing facilities (Figure 5), which was twice higher than the normal level (900 EU/mg of inhalable PM).

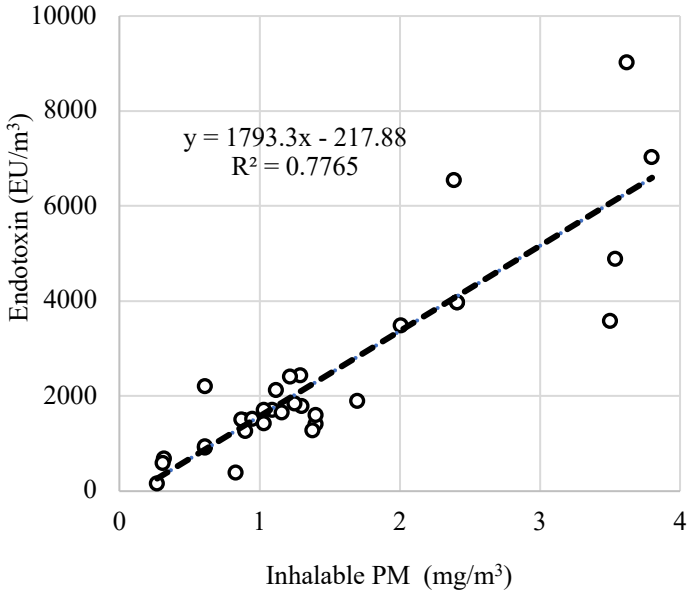

Figure 5. Concentrations of endotoxin vs. inhalable PM in finishing facilities

Endotoxin exposure levels in swine houses

The exposure levels of inhalable PM and endotoxins from task-based measurements in swine facilities are summarized in Table 1.

Table 1. Summary of exposure levels of inhalable PM and endotoxins from task-based measurements in swine facilities

	Inhalable PM (mg/m^3)		**Endotoxin (EU/m^3)**		**Endotoxin per mg of inhalable PM (EU/mg)**
	Median	Range	Median	Range	
All swine facilities	3.4	1 to 6	1906	400 to 6500	900
Feeding activities	4.5	2 to 6	3800	1100 to 6200	1800
Finishing facilities	1.3	1 to 4	1853	920 to 5400	1800
Power washing				5400 to 180900	
Hog load-out		2 to 31		3500 to 84400	2200
Outdoor		0.1 to 0.3		3 to 30	

8.3 Health effects assessment

No-Observed-Effect-Level (NOEL)

A variety of contaminants, microbial agents, and health effects associated with swine production have been documented in both occupational and community studies (Cole et al., 2000). Increased risks for bronchitis, COPD (Chronic obstructive pulmonary disease), and reduced FEV_1 (forced expiratory volume in one second) have been reported in swine farmers (Omland, 2002; Eduard et al., 2009). The inhalation of endotoxins triggers an inflammatory reaction in the lungs, which is characterized by the arrival of neutrophils and elevated levels of cytokines in the bronchoalveolar region (DECOS, 2010). Both short-term and long-term inhalation exposure to endotoxins are associated with a reduction in lung function, which is considered a critical effect.

The most reliable way to measure changes in lung function is by using FEV_1, which represents the amount of air that can be exhaled forcibly within one second. A difference between pre-exposure and post-exposure FEV_1 within a single day indicates acute effects, whereas a change in the baseline FEV_1 or a decrease in the annual FEV_1 is indicative of chronic effects. FVC (forced vital capacity) is the total amount of air that can be expired with force after full inspiration (measured in liters). The ratio FEV_1/FVC shows the amount of the FVC that can be expelled in one second.

The health impact that appears to be most susceptible is acute and chronic bronchial obstruction, which can be assessed by a reduction in FEV_1. Acute effects are quantified by the change in FEV_1 during exposure on a single day, denoted as ΔFEV_1. For instance, the difference in FEV_1 measured prior to and after a 4 or 8-hour work shift is referred to as the "across-shift ΔFEV_1." To determine FEV_1, the spirometer measurement is converted into a percentage of the predicted normal value that is standardized based on factors such as height, age, gender, and race. Chronic effects are evaluated by the average change in FEV_1 over the course of a year (annual FEV_1 change).

FEV_1 values define the degree of obstruction as following (Pat, 2022):

- FEV_1 greater than 80% of predicted = normal
- FEV_1 65% to 79% of predicted = mild obstruction
- FEV_1 50% to 64% of predicted = moderate obstruction
- FEV_1 less than 50% of predicted = severe obstruction

The endotoxin concentrations and corresponding across-shift ΔFEV_1 data in the literature are summarized in Table 2.

Table 2. Dose - response (ΔFEV_1 vs. endotoxin dose) data from the literature

Endotoxin concentration (EU/m^3)	Endotoxin dose (EU)	ΔFEV_1 (%)	NOEL (EU/m^3)	Notes	Reference
3230	16150	12.2	330	15 smoking cotton mill workers, including 8 had byssinosis, were exposed to cotton dust for 4 hours in an experimental card room on a Monday morning.	Rylander et al., 1985
1930	9650	9			
200	1000	2			
8030	40150	13			
480	2400	3.5			
3230	16150	8.5			
100	500	1			
5830	29150	14.7			
320	1600	8.8			
160	800	2.5			
5110	25550	31			
280	1400	16			
1040	5200	28			
60	450	0.1	90	108 different exposure sessions, healthy volunteers (24-35 subjects) were exposed to airborne dust generated by carding cotton for 6 hours	Castellan et al., 1987
80	600	0.5			
100	750	0			
500	3750	1.4			
1000	7500	4.5			
1500	11250	5			
2500	18750	8			
2800	21000	8.5			
7790	58425	9			
9300	46500	2.7	1700	11 subjects of non- smoker cotton mill workers exposure over the shift	Haglind & Rylander, 1984
26000	130000	2.5			
16300	81500	10			
7300	36500	20.3	800	17 subjects of smoker cotton mill workers exposure over the shift	
7300	36500	14.3			
2400	12000	2.7			
800	4000	3.2			
614	2302	3		257 poultry workers - over the shift exposure measurement lasting 2 to 4 hours	Donham et al., 2000
329	1645	6.24		205 dairy and 45 control (vegetable processing) workers - pre-and post-shift spirometry and interviews.	Mitchell et al., 2015
118	590	0		62 dairy parlor workers - Pre and post shift spirometry, questionnaire	Nonnenmann et al., 2017
600	3000	4.5	1800	Area sampling of swine confinement workers: 41 non-smokers and 16 smokers.	Donham et al., 1989
1300	6500	2.0			
2000	10000	4.0			
2500	12500	4.5			
3300	16500	7.0			
	555000	15	< 500	9 healthy persons exposed to buffered saline followed by inhalation with increasing doses of LPS in laboratory on weekly basis.	Michel et al., 1997
	415000	20		72 healthy persons exposed to buffered saline followed by inhalation with increasing doses of LPS in laboratory	Kline et al., 1999
			566	Estimated from all available data in the literature	

Note: Endotoxin dose = inhalable endotoxin concentration × exposure time × inhalation rate.

The No-Observed-Effect-Level (NOEL) was calculated as the endotoxin concentration at which average FEV_1 changes were zero, through regression using all the available data in the literature (Table 2). The regression equation is:

$$\ln(\text{endotoxin concentration}) = 0.1209\ (FEV_1) + 6.3881$$

The endotoxin concentration corresponding to zero FEV_1 decrease = exp (6.3881) = 595 EU/m^3. The NOEL of 595 EU/m^3 was based on FEV_1 measurements over one working shift of 3 to 6 hours. Recent studies among healthy volunteers and workers demonstrated symptoms and lung function changes to occur frequently at endotoxin levels between 100 and 200 EU m^{-3} (Smit et al., 2008; Basinas et al., 2012). A more conservative recommended exposure level (REL) for endotoxin was suggested by an expert committee associated with the Health Council of the Netherlands (HCN, 2010). That committee proposed an 8-h TWA of 90 EU/m^3 based on their conclusion that this value represented a no-observed-effect level (NOEL) for a worker inhaling that level of endotoxin over a 40-year work life.

Dose-response analysis

Human occupational inhalation rates in the literature are summarized in Table 3. Endotoxin doses for swine workers were calculated using the following equation. Human occupational default inhalation rate of 1.25 m^3/h was used.

$$\text{Endotoxin dose} = \text{inhalable endotoxin concentration} \times \text{exposure time} \times \text{inhalation rate}$$

Table 3. Human occupational inhalation rate

Human occupational default minute volume inhalation rate	1.25 m^3/h	EPA,2011
Human ambient default inhalation rate	0.83 m^3/h	EPA, 1994
Physiological daily inhalation rate (male adult)	0.92 m^3/h	Brochu et al., 2006b
Physiological daily inhalation rate (female adult)	0.71 m^3/h	Brochu et al., 2006b
Light activity average of daily inhalation rate (male adult)	1.2 m^3/h	ICRP,1981
Light activity average of daily inhalation rate (female adult)	1.14 m^3/h	ICRP,1981

Using a four hour daily working shift, and the median endotoxin concentration in swine facilities (1906 EU/m^3), the typical daily endotoxin dose for swine workers was estimated to be 9530 EU. During feeding activities, the typical daily endotoxin dose was estimated to be 19,000 EU. Activities like power wash can increase daily endotoxin dose to as high as 904,500 EU.

Dose-response curves (ΔFEV_1 vs. endotoxin dose) were developed for non-smokers and smokers respectively, using all the available data in the literature (Table 2). More uncertainties were observed in the dose-response relationship for smokers, and smokers were generally more sensitive to endotoxin dose (Figures 6 and 7).

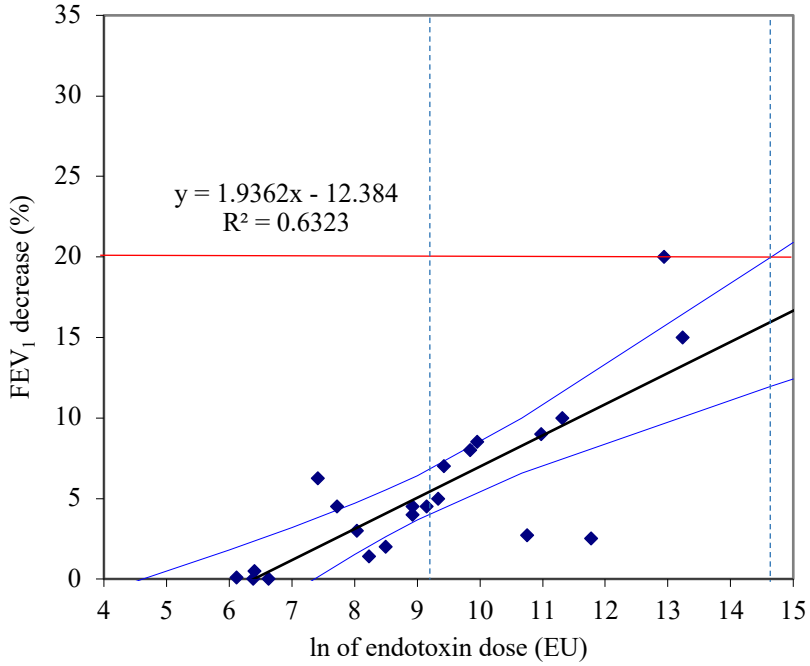

Figure 6. Dose-response curves (ΔFEV_1 vs. endotoxin dose) for non-smokers (The blue lines represent the 95% confidence interval)

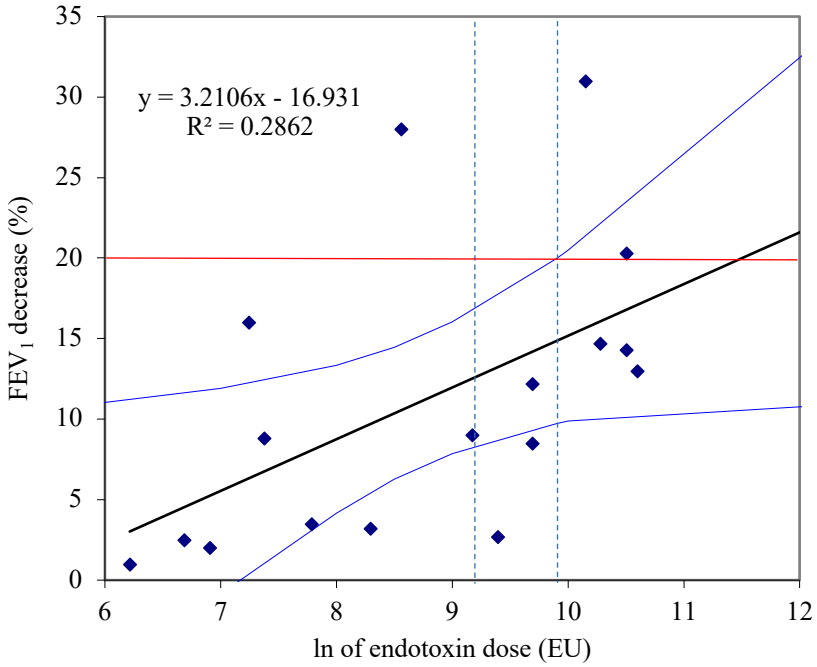

Figure 7. Dose-response curves (ΔFEV_1 vs. endotoxin dose) for smokers (The blue lines represent the 95% confidence interval)

As can be seen in Figure 6, the R^2 of the dose-response curve was 0.6323 for non-smokers. For every 2.718 times increase of endotoxin dose, the FEV_1 decreased 1.9 percentage points. At the typical daily

endotoxin dose for swine workers (9530 EU, ln of endotoxin dose = 9.14), the 95% confidence interval of FEV_1 decrease was from 3.9% to 6.7%. At the typical daily endotoxin dose for swine workers involved in feeding activities (19,000 EU, ln of endotoxin dose = 9.85), the 95% confidence interval of FEV_1 decrease was from 5.2% to 8.1%. For activities like power wash (with daily endotoxin dose as high as 904,500 EU, ln of endotoxin dose = 13.72), the 95% confidence interval of FEV_1 decrease was from 10.8% to 17.6%. For non-smokers, the endotoxin dose that has 2.5% chance of resulting $\Delta FEV_1>20\%$ was 2,300,000 EU.

As can be seen in Figure 7, the R^2 of the dose-response curve was 0.2862 for smokers. For every 2.718 times increase of endotoxin dose, the FEV_1 decreased 3.2 percentage points. At the typical daily endotoxin dose for swine workers (9530 EU, ln of endotoxin dose = 9.14), the 95% confidence interval of FEV_1 decrease was from 8.2% to 16.6%. At the typical daily endotoxin dose for swine workers involved in feeding activities (19,000 EU, ln of endotoxin dose = 9.85), the 95% confidence interval of FEV_1 decrease was from 9.6% to 16.7%. For activities like power wash (with daily endotoxin dose as high as 904,500 EU, ln of endotoxin dose = 13.72), the 95% confidence interval of FEV_1 decrease was from 12.7% to 41.5%. For smokers, the endotoxin dose that has 2.5% chance of resulting $\Delta FEV_1>20\%$ was 20,000 EU.

8.4 Risk characterization

Based on the results of exposure assessment and the dose-response analysis, the health risk levels associated with swine operations is summarized in Table 4.

Table 4. Summary of daily health risk levels associated with swine operations

	Endotoxin (EU/m^3)	**Endotoxin dose in a four hour working shift (EU)**	**Risk level**	**Notes**
Typical exposure level in swine facilities	1906	9,530	Low to medium	Much of the reported concentrations exceeded the calculated NOEL, 595 EU/m^3. Various respiratory symptoms may be observed, the 95% confidence interval of FEV_1 decrease is 3.9% to 6.7% for non-smokers and 8.2% to 16.6% for smokers. The chance of resulting $\Delta FEV_1>20\%$ is much lower than 2.5%.
Typical exposure level in feeding activities	3800	19,000	Low to medium	Exposure level in feeding activities is twice as higher as in other activities. The 95% confidence interval of FEV_1 decrease is 5.2% to 8.1% for non-smokers and 9.6% to 16.7% for smokers. The chance of resulting $\Delta FEV_1>20\%$ is much lower than 2.5%.
Maximum exposure level during power washing	180,900	904,500	Medium to High	Exposure level during power washing could be 50 times higher than in normal conditions. The 95% confidence interval of FEV_1 decrease is 10.8% to 17.6% for non-smokers and 12.7% to 41.5% for smokers. For smokers, the chance of resulting $\Delta FEV_1>20\%$ is larger than 2.5%. Use of personal protection equipment or reducing duration of high exposure are recommended.
Maximum exposure level during hog load-out	84,400	422,000	Medium to High	Exposure level during hog load-out could be 20 times higher than in normal conditions. The 95% confidence interval of FEV_1 decrease is 9.8% to 15.6% for non-smokers and 12.3% to 37% for smokers. For smokers, the chance of resulting $\Delta FEV_1>20\%$ is larger than 2.5%. Use of

				personal protection equipment or reducing duration of high exposure are recommended.
Outdoor	3 - 30		Very low	The reported concentrations are less than one-tenth of the calculated NOEL, 595 EU/m^3. They are also less than a more conservative recommended exposure level (90 EU/m^3), which represented a NOEL for a worker inhaling that level of endotoxin over a 40-year work life.

A long term individual-level risk is defined as the risk associated with an individual's exposure over a long period. It is calculated from the daily individual-level risk as:

$$\text{Long term risk} = 1-(1-P)^t$$

in which, P is the daily individual-level risk and t is the time exposed in days.

While there is evidence linking endotoxin to declines in lung function both over the long term and within a single work shift (Mitchell et al., 2015), there is no enough data in the literature to establish a clear dose-response curve for long term effect. It was reported that nearly 60% of swine confinement workers who have worked for 6 or more years' experience one or more respiratory symptoms (Clark et al., 1983; Donham et al., 1989). Assuming 350 working days per year, a 6-year term represents 2100 working days. When the long term risk accumulated in 6 years is 60%, using the long term risk equation, the daily risk is estimated to be 0.04%. This daily risk level agrees with the estimation in Table 4, which shows the daily risk level of resulting ΔFEV_1>20% is much lower than 2.5% with typical exposure level in swine facilities.

At daily risk of 0.04%, using the long term risk equation, the long term risk of experiencing one or more respiratory symptoms will be 13% for 1 year, 24% for two years, 34% for 3 years, 43% for 4 years, 50% for 5 years, and 57% for 6 years.

9. Discussion:

The inhalation of endotoxins triggers an inflammatory reaction in the lungs, which is characterized by the arrival of neutrophils and elevated levels of cytokines in the bronchoalveolar region (DECOS, 2010). Both short-term and long-term inhalation exposure to endotoxins are associated with a reduction in lung function, which is considered a critical effect. Based on FEV_1 measurements over one working shift of 3 to 6 hours, the NOEL of endotoxin exposure was estimated to be 595 EU/m^3, which corresponds to zero FEV_1 decrease. Endotoxin exposure levels in the literature were highly variable in swine facilities, ranging from 400 to 6500 EU/m^3. Much of the reported concentrations exceeded the estimated NOEL, 595 EU/m^3. Studies among healthy volunteers and workers demonstrated symptoms and lung function changes to occur frequently at endotoxin levels between 100 and 200 EU m^{-3} (Smit et al., 2008; Basinas et al., 2012). It has been observed that mucous membrane irritation occurs at levels of 200 - 500 EU/m^3, and acute bronchitis can occur at levels of 1000–2000 EU/m^3 (O'Shaughnessy et al., 2012). Symptoms like cough with phlegm, wheezing has been observed at levels of 90 - 220 EU/m^3. With the typical exposure level in swine facilities (median concentration = 1906 EU/m^3), various respiratory symptoms may be observed, but the resulting FEV_1 decreases are mostly less than 20%, which is still considered as normal (Pat, 2022). The chance of resulting ΔFEV_1>20%, which represents an obstruction in lung function, is much lower than 2.5%. Therefore, the overall daily health risk of reduced lung function associated with swine operations is considered to be low.

The majority of endotoxin are associated with inhalable PM instead of respirable PM. On average, in the task-based measurements, the concentrations of endotoxin in inhalable PM were about 36 times higher than that of respirable PM in swine facilities. This is reasonable since the main endotoxin sources are dust

particles from feed, manure, and animals, which are generally larger than the size range of respirable PM. Measurements of endotoxin concentration is not as easy as measurement of PM. When endotoxin measurements are not available, the concentration of endotoxin in swine facilities can be estimated by multiplying the concentration of inhalable PM with the estimated endotoxin level per mg of inhalable PM. It has been estimated that, on average, there were around 900 EU endotoxin per mg of inhalable PM in swine facilities. During feeding activities or in finishing facilities, the endotoxin levels increase to around 1800 EU per mg of inhalable PM.

Higher endotoxin levels were observed from task-based measurements during feeding activities, and in finishing facilities. Especially, in the situation of power washing and hog load-out, endotoxin exposure levels could be 20 to 50 times higher than in normal conditions. This will bring much higher daily health risk of reduced lung function.

Smokers were generally more sensitive to endotoxin exposure than non-smokers, and involves more uncertainties. For non-smokers, the endotoxin dose that has 2.5% chance of resulting ΔFEV_1>20% was 2,300,000 EU, while for smokers, the endotoxin dose that has 2.5% chance of resulting ΔFEV_1>20% was only 20,000 EU. In the situation of power washing and hog load-out, workers could experience endotoxin dose as high as 4 to 9 times higher than 20,000 EU. Therefore, for smokers, the chance of resulting ΔFEV_1>20% is larger than 2.5%. Use of personal protection equipment or reducing duration of high exposure are recommended in these situations.

The reported endotoxin concentrations in outdoor environment near swine facilities were 3 to 30 EU/m^3, which were less than one-tenth of the calculated NOEL, 595 EU/m^3. They are also less than a more conservative recommended exposure level (90 EU/m^3), which represented a NOEL for a worker inhaling that level of endotoxin over a 40-year work life. The health risk of reduced lung function for community neighbors associated with swine operations is low.

It has been reported that repeated or prolonged exposure to endotoxins can result in tolerance to acute effects (Greisman et al., 1969) which might obscure the actual dose-response curve. And there is some indication that this tolerance dissipates within a few days following the termination of exposure (DECOS, 2010). evidences of the dose-response relationship for individuals living near swine farms were inconsistent in literature. Few community studies reported an association between surrogate clinical outcomes and proximity to swine operations. There is no enough data in the literature to establish a clear dose-response curve for long term effect. However, long term risks could be estimated based on a reasonable estimation of daily risk, and the time exposed in days. Although the daily occupational and community risk of reduced lung function is low, the accumulated long term risk could be significant. Lung function measured as FEV_1 seems to be reduced in farmers compared to controls, and longitudinal studies indicated an increased annual loss in FEV_1 in swine farmers (Omland, 2002). At an estimated daily risk of 0.04%, the long term risks of experiencing one or more respiratory symptoms are estimated to be 13% for 1 year, 24% for two years, 34% for 3 years, 43% for 4 years, 50% for 5 years, and 57% for 6 years.

There are no standards for endotoxin exposure promoted by an agency in the USA. However, since much of the reported endotoxin concentrations exceeded the estimated NOEL, 595 EU/m^3. In order to protect health of swine workers, mitigation strategies may be considered to lower endotoxin exposure to be lower than the NOEL. Given the estimation of 900 EU endotoxin per mg of inhalable PM, the 595 EU/m^3 NOEL corresponds to inhalable PM concentration of 0.7 mg/m^3. In another word, when the inhalable PM concentration is larger than 0.7 mg/m^3, it is likely that the associated endotoxin concentration will be larger than the 595 EU/m^3 NOEL. Since the majority of endotoxin are associated with inhalable PM, any mitigation strategies that can reduce inhalable PM will contribute to the reduction of associated endotoxin concentration, which may include increasing fat content in feed, wet feeding, automated dry feeding, full concrete floor, oil spraying, ventilation, use of personal protection equipment, etc.

Appendix 1. Exposure data from task-based personal sampling measurements in literature

Activities	Inhalable PM and endotoxin			Respirable PM and endotoxin			Country	Analytical method	References
	PM (mg/m^3)	Endotoxin (EU/m^3)	Endotoxin /PM (EU/mg)	PM (mg/m^3)	Endotoxin (EU/m^3)	Endotoxin /PM (EU/mg)			
Not specified minimum	2.2	200	91	0.3	100	333	Sweden	LAL	Haglind & Rylander, 1987
Not specified maximum	15.2	19000	1250	1.4	300	214			
All	6.8	2400	353	0.34	2300	6765	Sweden	Gel Clot LAL assay	Donham et al. 1989
All Minimum	1.8	200	111						
All Maximum	21.7	11000	507	2.2	5600	2545			
All Spring	1.57	240	153				Netherlands	Gel Clot LAL assay	Heederik et al. 1990
All	4.01	1300	324				Netherlands	Gel Clot LAL assay	Heederik et al. 1991
All Minimum	0.47	310	660						
All Maximum	23.48	3430	146						
Feeding minimum	4.1	1940	473		90		Sweden	Gel Clot LAL assay	Larsson et al. 1992
Feeding maximum	13.7	7160	523		530				
Animal handling (tending)	7.4	370	50		80				
Animal handling (tending) minimum	10	220	22		50				
Animal handling (tending) maximum	27.3	600	22		290				
Feeding	13.8	3150	228		170				
Breeding minimum	1.12	90	80	0.18	10	56	Denmark	Chromogenic LAL assay	Christensen et al. 1992
Breeding maximum	6.76	1200	178	1.04	130	125			
Breeding	4.13	640	155	0.48	50	104			
Breeding	4	585	146	0.43	45.4	106	Denmark	Chromogenic LAL assay	Vinzents & Nielsen,, 1992
Animal handling (weighing)	14	4200	300				Sweden	Chromogenic LAL assay	Malmberg & Larsson, 1993
Animal handling (weighing)	6.9	2100	304						
Animal handling (weighing)	9.9	4000	404						
Animal handling (weighing) minimum	5.6	800	143				Sweden	Chromogenic LAL assay	Larsson et al. 1994
Animal handling (weighing) maximum	24	13000	542						
Animal handlin (weighing)	13.5	6000	444						
All subject	4.53	202.35	45	0.23	16.59	72	USA	Chromogenic LAL assay	Donham et al. 1995
All (0 -6*)	3.9	135.64	35	0.19	18.51	97			
All (7-9*)	5	244.69	49	0.19	18.15	96			
All (10-13*)	5.64	340.36	60	0.23	17.89	78			
All (>14*)	5.37	170.72	32	0.28	13.03	47			
Breeding & Finishing (all season)	2.4	920	383				Netherlands	Kinetic Limulus Amebo-cyte Lysate (LAL) assay	Preller et al. 1995
Breeding & Finishing (winter)	2.6	1090	419						
Breeding & Finishing (summer)	2.2	780	355						
Breeding & Finishing Minimum (winter)	0.3	106	353						
Breeding & Finishing Maximum (winter)	26.6	15030	565						
Breeding & Finishing Minimum (summer)	0.5	56	112						
Breeding & Finishing Maximum (summer)	11.2	8250	737						
All	4.55	202.7	45	0.23	16.95	74	USA	Endpoint Chromogenic LAL assay	Reynold et al., 1996
All	3.45	176.1	51	0.26	11.86	46			
All (0 -6*)	3.73	132.85	36	0.2	18.51	93			
All (7-9*)	5.4	239.46	44	0.21	18.15	86			
All (10-13*)	5.16	309.6	60	0.24	17.89	75			
All (>14*)	4.45	159.49	36	0.26	13.03	50			
All (0 -6*)	3.32	129.83	39	0.31	5.57	18			
All (7-9*)	3.9	140.17	36	0.3	13.28	44			

All (10-13*)	3.24	260.09	80	0.22	11.27	51			
All (>14*)	3.43	159.09	46	0.26	13.58	52			
Weighing minimum	20	11000	550				Sweden	Chromogenic LAL assay	Larsson et al. 1997
Weighing maximum	29.3	14000	478						
Weighing	23.3	13000	558						
Grower-Finisher	2.41	3983.5	1653				Canada	Kinetic Chromogenic LAL assay	Senthilselvan et al. 1997
All	2.7	1110	411				Netherlands	Kinetic LAL assay	Vogelzang et al. 1997
All	2.63	1050	399				Netherlands	Kinetic LAL assay	Vogelzang et al. 1998
Grower-finisher	2.41	3984	1653				Canada	Chromogenic LAL assay	Zhang et al 1998
Breeding minimum	0.76	600	789				UK	Kinetic turbidimetric LAL assay	Simpson et al. 1999
Breeding maximum	19.09	149230	7817						
Breeding	6.71	6310	940						
Breeding	5.78	6600	1142						
Feeding				0.3	67	223	Germany	Kinetic turbidimetric LAL assay	Radon et al. 2000
Feeding Maximum				39.6	4444	112			
Not specified	2.63	1050	399				Netherlands	LAL	Vogelzang et al_2000
Not specified	2.58	1050	407						
Not specified	2.65	1060	400						
Animal handling (tending)	3.1	23000	7419				Norway	KLARE (Kinetic Limulus assay with resistant-parallel-line estimation	Melbostad & Eduard 2001
All median	4	580	145				Demark	Kinetic turbidimetric LAL assay	Radon et al. 2001
All minimum	1.1	13	12						
All maximum	13.8	11017	798						
All median	5	763	153				Germany	Kinetic turbidimetric LAL assay	Radon et al. 2002
All maximum	76.7	20901	273						
All minimum	1.6	992	620				Netherlands	Kinetic Chromogenic LAL assay	Spaan et al. 2006
All maximum	5.4	6970	1291						
All	2.6	1510	581						
All		3400					Netherlands	Chromogenic LAL assay	Smit et al. 2008
Finishing minimum (Summer)	0.61	2218	3636				Canada	Endpoint Chromogenic LAL assay	Bonlokke et al. 2009
Finishing maximum (Summer)	10.24	25861	2525						
Finishing (Summer)	2.39	6553	2742						
Finishing minimum (Winter)	1.3	1800	1385						
Finishing minimum (Winter)	7.8	69096	8858						
Finishing (Winter)	3.8	25690	6761						
Grower-Finisher	0.89	1500.1	1686				Canada	Kinetic Chromogenic LAL assay	Senthilselvan et al. 2009a
Grower-Finisher	0.87	1509.7	1735						
Grower-Finisher Minimum	0.61	923.8	1514						
Grower-Finisher Maximum	1.29	2436.7	1889						
Grower-Finisher Minimum	0.61	942.7	1545						
Grower-Finisher Maximum	1.22	2417.7	1982						
Grower-Finisher	0.9	1267	1408				Canada	Kinetic Chromogenic LAL assay	Senthilselvan et al. 2009b
Grower-Finisher	1.7	1906	1121						
Grower-Finisher	1.4	1420	1014						
Grower-Finisher	1.4	1605	1146						
Gestation/farrowing GM (summer)	0.83	400	482				USA	Kinetic Chromogenic LAL assay	O'Shaughnessy et al. 2009
Gestation/farrowing GM (winter)	3.76	2500	665						
Finishing minimum (Hog load-out)	2.01	3497	1740						

Finishing maximum (Hog load-out)	31.06	84357	2716						
Finishing (Hog load-out)	7.14	12150	1702						
Finishing minimum (Power Washing)		5401							
Finishing maximum (Power Washing)		180864							
Finishing (Power Washing)		40353							
All (summer)	2.8	1090	389				Denmark	Kinetic Chromogenic LAL assay	Basinas et al. 2012
All (winter)	4.1	2080	507						
All	3.4	1490	438						
All (summer)	4.3	5950	1384						
All (winter)	5.5	6550	1191						
All	4.9	6240	1273						
Feeding (indoor)	4	1800	450				Denmark	Kinetic Chromogenic LAL assay	Basinas et al. 2013
Feeding (indoor summer)	3.4	1400	412						
Feeding (indoor winter)	4.8	2400	500						
Feeding (indoor)	5.3	5300	1000						
Feeding (indoor summer)	4.7	5200	1106						
Feeding (indoor winter)	5.9	5300	898						
Feeding	3.4	1500	441						
Feeding (summer)	2.8	1100	393						
Feeding (winter)	4.1	2100	512						
Feeding	4.9	6200	1265						
Feeding (summer)	4.3	6000	1395						
Feeding (winter)	5.5	6000	1091						
All	1.69	2026	1199				USA	Kinetic Chromogenic LAL assay	Sauve et al 2020

Appendix 2. Exposure data from stationary sampling measurements in literature

Facility type Location	Inhalable PM and endotoxin			Respirable PM and endotoxin			Country	Analytical method	Reference
	PM (mg/m^3)	Endotoxin (EU/m^3)	Endotoxin /PM (EU/mg)	PM (mg/m^3)	Endotoxin (EU/m^3)	Endotoxin /PM (EU/mg)			
Not specified	4.63	2800	605				Sweden	Gel Clot LAL assay	Clark et al. 1983
Not specified	3.8	600	158						
Not specified	2	1200	600						
Not specified	1.76	500	284						
Not specified	2.82	400	142						
Not specified	1.82	700	385						
Not specified	5.17	2200	426						
Not specified	2.64	1000	379						
Overall	3.08	1200	390						
All	4.3	1800	419	0.33	1700	5152	Sweden	Gel Clot LAL assay	Donham et al. 1989
All Minimum	1.4	400	286		100				
All Maximum	8.3	3300	398		5600				
Grower/Finishing	11.18	46	4				UK	Gel Clot LAL assay	Crook et al. 1991
Grower/Finishing	9.92	173	17						
Grower/Finishing	3.99	285	71						
Grower/Finishing	3.82	19	5						
Grower/Finishing	3.11	243	78						
Farrowing	3.03	125000	41254				Poland	Gel Clot LAL assay	Dutkiewicz et al. 1994
Farrowing	3.35	312500	93284						
Farrowing	14.05	18800	1338						
Fattening	4.1	312500	76220						
Fattening	6.25	750000	120000						
All Median	2.77	5427	1959	0.12			Canada	Gel Clot LAL assay	Zejda et al. 1994
All Minimum	1.71	438	256	0.05					
All Maximum	5.02	41307	8228	0.32					
All	21	12000	571						Wang et al. 1996
Grower-Finisher	3.8	7030	1850				Canada	Kinetic Chromogenic LAL assay	Senthilselvan et al. 1997
Fattening daytime		1115			145		UK	Gel Clot LAL assay	Seedorf et al 1998
Fattening daytime		2047			208		Denmark		
Fattening daytime		1361			121		UK		
Fattening daytime		1022			108		Netherlands		
Fattening daytime		1287			76		Denmark		
Fattening daytime		1345			101		Germany		
Fattening nighttime		1565			53		UK		
Fattening nighttime		1513			212		Denmark		
Fattening nighttime		758			75		UK		
Fattening nighttime		1002			143		Netherlands		
Fattening nighttime		712			78		Denmark		
Fattening nighttime		649			107		Germany		
All	4	588	147		45.4				Vogelzang et al. 1998
Finishing	3.54	4900	1384				Canada	Chromogenic LAL assay	Duchaine et al., 2000
Open-style Breeding	0.15	36.8	245	0.12	14.1	118	Taiwan	KLARE (Kinetic Limulus assay with resistant-parallel-line estimation	Chang et al. 2001
Open-style Breeding Minimum	0.009	15.8	1756	0.01	3.4				
Open-style Breeding Maximum	0.23	73.2	318	0.49	56.6				
Partially-enclosed Farrowing	0.23	82.1	357	0.08	48.6	608			
Partially-enclosed Farrowing Minimum	0.08	14.4	180	0.01	3.5				
Partially-enclosed Farrowing Maximum	0.47	277	589	0.22	837				
Partially-enclosed Nursery	0.34	298	876	0.13	20.9	161			
Partially-enclosed Nursery Minimum	0.16	32	200	0.02	1.6				
Partially-enclosed Nursery Maximum	0.54	818	1515	0.57	155				
Open-style Growing	0.28	145	518	0.15	21.8	145			
Open-style Growing Minimum	0.03	40.1	1337						
Open-style Growing Maximum	1.11	298	268	0.64	217				

Open-style Finishing	0.21	136	648	0.24	129	538			
Open-style Finishing Minimum	0.09	30.8	342	0.03	5.6				
Open-style Finishing Maximum	0.34	418	1229	1.45	1643				
All stages Overall	0.24	140	583	0.14	47	336			
All stages Overall Minimum	0.03	14.4	480						
All stages Overall Maximum	1.11	818	737	1.45	1643				
Outdoor mean	0.12	8.9	74	0.12	14.1	118			
Outdoor Minimum	0.06	3.2	53						
Outdoor Maximum	0.31	32.9	106						
Finishing Median		668.7			23.1		Germany	Chromogenic LAL assay	Schierl et al 2007
Finishing Minimum		43.2			18				
Finishing Maximum		7469			236				
Grower-finisher	1.09	1722	1580				Canada	LAL assay	Lavoie et al 2009
Grower-finisher	1.12	2140	1911						
Grower-finisher	0.95	1530	1611						
Grower-finisher	1.03	1720	1670						
Grower-finisher	1.03	1430	1388						
Grower-finisher	1.25	1850	1480						
Grower-finisher	1.16	1660	1431						
Finisher (slatted floor)	1.24	26700	21532				Canada	Endpoint Chromogenic LAL assay	Létourneau et al 2009
Finisher (sawdust floor)	1.24	51900	41855						
All		636					Switzerland	Kinetic Chromogenic LAL assay	Masclaux et al 2013
All Minimum		17							
All Maximum		6149							
All winter		2666							
All Mnimum winter		721							
All Maximum winter		6149							
All summer		444							
All Minimum summer		17							
All Maximum summer		2678							
Farrowing	0.76	334	439				USA	Kinetic Chromogenic LAL assay	Yang et al 2013
Farrowing Minimum	0.24	98	408						
Farrowing Maximum	2.27	2099	925						
Gestation	0.67	419	625						
Gestation Minimum	0.3	164	547						
Gestation Maximum	1.39	991	713						
Weaning	1.16	1017	877						
Weaning Minimum	0.14	217	1550						
Weaning Maximum	4.59	8702	1896						
Finishing	1.38	1285	931						
Finishing Minimum	0.32	693	2166						
Finishing Maximum	3.5	3588	1025						
Farrowing	0.34	200.9	591	0.13	46.8	360	USA	Kinetic Chromogenic LAL assay	Yang et al 2014
Gestation	0.17	63.9	376	0.06	20.5	342			
Weaning	0.28	148.2	529	0.07	22.8	326			
Finishing	0.27	162.7	603	0.16	64.1	401			
Open house (all)	0.87	443.18	509	0.67	7.22	11	Korea	Kinetic Limulus Amebo-cyte Lysate (LAL) assay	Roque et. al. 2018
Open house (all) Minimum	0.1	47.1	471	0.28	0.55	2			
Open house (all)	1.54	1198.8	778	0.83	14.48	17			
Open house (all)	0.58	13	22	0.32	1.03	3			
Open house (all) Minimum	0.13	0		0.01	0.01	1			
Open house (all) Maximum	1.06	29.6	28	0.96	2.76	3			
Finishing	3.62	9030	2494				Canada	Kinetic Chromogenic LAL assay	Pilote et al 2019
Finishing Minimum	0.309	602	1948						
Finishing Maximum	9.61	34000	3538						

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