Health effects associated with exposure to hazardous biological agents and their constituents in poultry farming

ABSTRACT

Introduction: Poultry workers are at increased risk of respiratory disorders as a result of exposure to organic dust, microorganisms and their microbial cell wall agents. Previous studies have revealed that farm workers experienced respiratory symptoms such as cough, phlegm and wheezing, while some developed asthma and toxic pneumonitis. The aim of this review is to highlight the health effects associated with poultry dust exposure of various poultry job categories. It also aims to promote awareness on measures that could be implemented to minimise the burden of respiratory disease.

Methodology: A literature review of scientific papers (1980-2010) related to biological hazards in poultry settings was conducted. The search was done using Google, major occupational health journals and information from credible occupational health and safety institutes.

Results: The paper presents a review of the potential health effects associated with occupational exposure to poultry dust and hazardous biological agents in poultry farming. The review also discusses the emerging biological agents found in poultry settings that have been associated with work-related respiratory disorders.

Conclusion: Poultry dust exposure appears to have an effect on the respiratory response of workers. An understanding of exposure to multiple biological agents associated with poultry farming is critical in reducing respiratory disorders thus creating a safe environment for employees. Further studies on dose response relationships and OELs are required.

Keywords: poultry, hazardous biological agents, health effects, dust, exposure, occupational, bacteria, fungi, virus, endotoxin, (1-3) β-D-glucan, MVOCs, allergens

INTRODUCTION

The poultry industry continues to dominate the South African livestock sector as chicken remains an affordable protein source compared to other meat products. The South African poultry industry mainly includes chicken farming (e.g. broiler and egg) and processing. This industry is still an important contributor to employment opportunities both in the formal and informal sector with 80% of the industry comprising small, medium and micro enterprises which employ approximately 77 000 people, although not all are involved in farming.

Poultry farmers spend considerable periods of time in their work environments and are therefore at risk of exposure to very high levels of poultry dust. Poultry dust is defined as a complex mixture of dust, which includes feed and litter and/or bedding particles, feathers, faeces, mites, microorganisms (e.g. bacteria, fungi and viruses) and their biological constituents (e.g. endotoxin, (1-3) β-D-glucan, mycotoxins) and skin scales. The solid portion of dust acts as a carrier for biological contaminants and toxic gases (e.g. ammonia and carbon dioxide), which then get inhaled into the lungs. These contaminants vary in poultry operations and may be influenced by bird age and densities, ventilation rates, microclimatic parameters (e.g. humidity and temperature), types of litter and feed, type and size of poultry housing and job tasks.

Although the poultry industry is technically a well controlled environment (e.g. animal health and hygiene practices), studies from different countries have demonstrated a high prevalence of both upper and lower respiratory symptoms and decreased lung function in poultry workers. The type of production (cage versus floor) also appears to influence the health outcome, with cage-operation workers demonstrating a higher prevalence of respiratory symptoms and decreased lung function in poultry workers. The type of production (cage versus floor) also appears to influence the health outcome, with cage-operation workers demonstrating a higher prevalence of respiratory symptoms.

Only one study focusing on occupational exposure in the South African poultry sector has been reported thus far. This study investigated work-related respiratory symptoms in...
poultry workers and found a very high prevalence of exposure-related symptoms associated with organic dust exposure. However, specific causative agents were not identified which is important as this would assist in management of affected workers. A further limitation of this study was the lack of objective exposure assessments and the inability to demonstrate an association between allergic sensitisation and respiratory symptoms.

The main purpose of this paper is to describe the health effects associated with occupational exposure to hazardous biological agents (HBAs) and their constituents in poultry farming. In addition, it also aims to promote awareness about reducing exposure to poultry workers. The various methodologies used to detect and/or quantify these agents are explored. The limitations where relevant are described.

**METHODOLOGY**

Studies on occupational hazards associated with HBAs and their constituents in the poultry industry (1980-2010) were searched through Google. The keywords used included poultry, chicken, hazardous biological agents, health effects, dust, exposure, occupational, bioaerosols, bacteria, fungi, virus, endotoxin, (1-3) β-D-glucan, microbial volatile organic compounds (MVOCs), mites, 21st century, avian flu and allergens. Major peer-reviewed occupational health journals and reports from credible international occupational health and safety institutions (e.g. Health and Safety Executive-UK and National Institute for Occupational Safety and Health-USA) were also used for the search.

Only selected publications were used after evaluation, as this review focussed on the influence of biological agents and their constituents on the health of poultry workers. The various methodologies used to detect and/or quantify these agents are explored. The limitations where relevant are described.
workers. The search was therefore narrowed as some publications mainly focussed on the health of the chickens or birds and food safety while others discussed the non-biological pollutants (e.g. ammonia and carbon dioxide). However, microbial volatile organic compounds (MVOCs) were included in the search since they are mostly produced by fungi and may be suitable markers of fungal growth.

RESULTS

1. Source of exposure

   Poultry industries vary between countries, although some processes are similar to several or all sectors. Virtually every stage of work across the industry could result in exposure to biological agents of both permanent and contracted workers (Table 1).

   Table 1. General job categories of poultry workers and description of work performed and possible sources of exposure capable of causing irritation, respiratory sensitisation or disease.5,9

<table>
<thead>
<tr>
<th>Job category*</th>
<th>Description of duties</th>
<th>Source of exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laying litter/bedding</td>
<td>Spreading litter/bedding in poultry houses</td>
<td>Nature of material. Certain products carry fungal spores, inhalable dust.</td>
</tr>
<tr>
<td>Catchers</td>
<td>Repopulating and depopulating chicks/chickens</td>
<td>Proteins from feather debris or dander, mites (dust mites, storage mites), faecal residues, dust particles, airborne bacteria, endotoxin.</td>
</tr>
<tr>
<td>Litter/manure removal</td>
<td>Removing soiled litter</td>
<td>Inhalable dust organic compounds released during degradation of litter and feed.</td>
</tr>
<tr>
<td>Cleaning</td>
<td>Routine cleaning</td>
<td>Exposure to feathers, mites, feed particles.</td>
</tr>
<tr>
<td>Forklift drivers</td>
<td>Load boxes/cages of chicken into trucks for transportation to slaughterhouses.</td>
<td>Inhalable poultry dust.</td>
</tr>
</tbody>
</table>

   * Job categories may vary, depending on the type of farming and country.

2. Biological agents associated with exposure in poultry farms

   Biosecurity is an integral part of the poultry industry. Workers and visitors to farming operations often have to shower and put on other clothes before they are allowed to come in contact with the chickens. The entire operation is fenced in, access control is applied, and all traffic (humans and vehicles) is monitored to ensure the health of the animals and workers.10

   Nonetheless, in poultry farming, bacteria, endotoxin, and fungi contaminants are the highest compared to other animal farming.11 Other biological contaminants such as mites12,13 and (1-3) β-D-glucan14,15 have been detected in poultry settings, albeit a paucity of information is available. The zoonotic diseases and infections naturally transmitted between vertebrate and human are also common.

   Some of these contaminants form part of the natural flora of the animals and the litter or bedding material used while others are due to feed contamination and management processes such as storage facilities and procedures. On the other hand others appear as emerging risks (e.g. (1-3) β- D-glucans, MVOCs and mites) as new scientific knowledge on the topic comes to light, particularly with respect to mixed exposures and synergistic effects.9
2.1. **Bacteria:** The most common bacteria found in poultry facilities which are known to cause respiratory effects and/or infections in workers include *Pseudomonas sp*, *E.coli sp*, *Staphylococcus sp*, *Bacillus sp*, *Microcococcus sp*, *Proteus sp* and *Clostridia sp*.\(^2\) The determination of bacteria is usually done by culture methods in air samples collected by impaction on agar plates or in surface dust samples and reported as CFU/m\(^3\) air or CFU/m\(^2\) surface, respectively. Recent studies used quantitative polymerase chain reaction (PCR) for airborne bacterial quantification in poultry houses,\(^5\) however the validity of this method as a tool for quantitative exposure assessment for bioaerosols needs to be evaluated.\(^5\)

2.2. **Fungi:** Fungi in poultry facilities that are capable of causing respiratory disorders include: *Aspergillus sp*, *Penicillium sp*,\(^2\) *Cladosporium sp*, *Histoplasma capsulatum* and less commonly *Alternaria sp*, *Fusarium sp*, *Geotrichum sp* and *Streptomyces sp*.\(^12,16\) As part of their normal metabolism, fungi can produce a variety of volatile organic compounds (VOCs) (see section 3.3) and are emitted during the composting of poultry litter. Airborne fungal concentration can be measured by impaction onto mould agar, cultured and expressed as CFU/m\(^3\). Alternative methods include microscopy using staining techniques\(^5\) and spore counting by estimating the microbial cell wall agents (MCWAs) (e.g. (1-3) β-D-glucan). The application of PCR and probe hybridisation techniques in detection of airborne fungal spores in environmental samples is still in its infancy stage.\(^17-19\)

2.3. **Viruses:** The well known viral disease and the highly pathogenic avian influenza (HPAI) H5N1 viruses which occur in poultry (e.g. chickens) have infected humans in many countries. The H5N1 viral infection of humans associated with direct poultry contact are rare however the mortality rate is high.\(^20\) As for viruses, exposure assessments have hardly been developed for occupational environments. Human exposure to H5N1 virus is often on collection of specimen samples for epidemiological data management of the disease. There is therefore a need for environmental sampling protocols that can provide researchers with well documented, representative samples of exposure.\(^21\)

2.4. **Mites:** Occupational health risks of exposure to mites are not well defined in the poultry industry.\(^11,12\) The dust mites *Dermatophagoides evansi*, *D. farinae*, *D. pteronyssinus*, *Euroglyphus longior*, *Thyreophagus entomophagus* and *Lepidoglyphus destructor* were identified in dust samples from poultry farms, with the latter being the most abundant mite.\(^22\) A recent study found hazardous levels of *D. pteronyssinus* (Der p1) in poultry houses.\(^12\) Apart from the poultry dust, the Northern Fowl Mite (*Ornithonyssus sylviarum*) inhabiting chicken feathers may be a predominant allergen causing occupational allergy in poultry workers.\(^13\) This is not commonly tested in South Africa which may lead to underestimation of the levels of the agent. The mites’ concentration in

---

**“Poultry workers have an increased incidence of respiratory symptoms and a decline in lung function related to exposure to organic dust.”**
the dust is analysed by microscopy and reported as mite units/m³. Dust can also be sampled onto filters by air filtration with a pump. A range of quantitative antibody-based immunoassays, particularly enzyme-linked immunosorbent assays (ELISA) for allergens from dust mite such as *D. pteronyssinus*, *D. farinae* and *Blomia tropicalis* has been manufactured recently (Indoor Biotechnologies Inc, 2009) and needs to be further researched for routine application.

3. **Constituents of biological agents**

The biological agents of microbial origin may include the organism itself (e.g. bacteria, fungi and viruses), toxins (e.g. endotoxin produced by Gram-negative bacteria and mycotoxins produced by fungi), cell wall constituents such as (1-3) β-D-glucans produced by fungi, or enzymes produced by genetic modification of microorganisms.

3.1. **Endotoxin**: Endotoxins (also referred to as lipopolysaccharides) are components of the external membrane of most Gram-negative bacteria. Endotoxins are responsible for many of the virulent effects of Gram-negative bacteria. Although poultry dust consists of a mixture of contaminants, endotoxin is thought to be the major component of the dust. The type, duration, and level of exposure to endotoxins varies greatly between poultry farming and production exceeding the suggested threshold value of 100 EU/m³ for airways inflammation. This evidence is a cause for the concern of the well-being of workers, therefore methods to reduce exposure are needed. Workplace monitoring of endotoxins is usually performed by sampling airborne inhalable dust onto filter membranes with a subsequent aqueous extraction. Endotoxin is then analysed using the chromogenic-endpoint limulus amoebocyte lysate (LAL) assay which measures the biological activity of endotoxin and reported as endotoxin units per 1m³ (EU/m³). Endotoxin can also be measured by gas chromatography-mass spectrometry.

### Table 2. Biological agent exposure and health effects of poultry workers

<table>
<thead>
<tr>
<th>Country</th>
<th>Sample size</th>
<th>Exposure</th>
<th>Respiratory health effects</th>
<th>Prevalence / OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Croatia12</td>
<td>41</td>
<td>Total dust (0.4 - 1.1 mg/m³), Mites (&lt;0.1 - 3.3 mg/g), Fungi (4.9x10⁴ - 6.8x10⁵ CFU/m³), Endotoxin (230 – 284 EU/m³)</td>
<td>Eye symptoms</td>
<td>34%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Nose symptoms</td>
<td>39%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Asthma symptoms</td>
<td>39%</td>
</tr>
<tr>
<td>Canada2</td>
<td>111</td>
<td>Total dust (8.6 mg/m³), Endotoxin (8514 EU/m³)</td>
<td>Chronic phlegm</td>
<td>19%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Chronic wheeze</td>
<td>16%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Chronic cough</td>
<td>13%</td>
</tr>
<tr>
<td>Brazil38</td>
<td>473</td>
<td>Poultry dust</td>
<td>Asthma symptoms</td>
<td>1.1 (0.6 - 1.9)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Chronic respiratory symptoms</td>
<td>1.6 (1.1 - 2.5)</td>
</tr>
<tr>
<td>Sweden15</td>
<td>42</td>
<td>Endotoxin (410 ng/m³), (1-3) β-D-glucan (270 ng/m³)</td>
<td>Decreased lung function</td>
<td>n/r</td>
</tr>
<tr>
<td>Switzerland11</td>
<td>37</td>
<td>Poultry dust</td>
<td>Wheezing</td>
<td>2.7 (0.7 - 10.6)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Chronic bronchitis</td>
<td>0.9 (0.3 - 3.1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Phlegm</td>
<td>1.1 (0.4 - 3.2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Asthma-related symptoms</td>
<td>2.9 (0.9 - 9.6)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Nasal allergy</td>
<td>3.0 (1.0 - 37.7)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Nasal irritation</td>
<td>5.3 (1.6 - 18.0)</td>
</tr>
<tr>
<td>Switzerland7</td>
<td>36</td>
<td>Total dust (7 mg/m³), Bacteria (4.7x10⁹ CFU/m³), Fungi (2.0x10⁷ n/m³), Endotoxin (258 ng/m³)</td>
<td>Decreased lung function</td>
<td>n/r</td>
</tr>
<tr>
<td>Iowa28</td>
<td>257</td>
<td>Total dust (2.4 mg/m³), Respirable dust (0.16 mg/m³), Endotoxin (814 EU/m³)</td>
<td>Greater cross-shift (before and after work) decline in FEV₁</td>
<td>n/r</td>
</tr>
<tr>
<td>New Zealand43</td>
<td>1706</td>
<td>Poultry dust</td>
<td>Asthma</td>
<td>17.4%</td>
</tr>
<tr>
<td>South Africa8</td>
<td>134</td>
<td>Poultry dust</td>
<td>Work-related cough</td>
<td>32%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Work-related wheeze</td>
<td>23%</td>
</tr>
<tr>
<td>Israel13</td>
<td>16</td>
<td>Poultry-related antigens</td>
<td>Rhinitis</td>
<td>94%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Asthma</td>
<td>88%</td>
</tr>
</tbody>
</table>

FEV₁ – forced expiratory volume in 1 second, EU – Endotoxin units, OR (95% CI) – odds ratio (95% confidence interval), n/r – not reported
spectrometry (GC-MS). Owing to different measurement protocols, large inter-laboratory variations in the results exist. Therefore, the need for standardisation of methods is supported by many researchers. Due to the inherent variability, it is recommended that endotoxin air levels be monitored more frequently than normally applied for workplace control measurements.

3.2. (1-3) β-D-glucan: (1-3) β-D-glucan is a non-allergenic water insoluble cell wall component of most fungi, some bacteria and plants and can be found in organic dust. (1-3) β-D-glucan has been used as a surrogate measure for fungi exposure in airborne studies and has previously been measured in poultry farms ranging from 2 – 972 ng/m³. Airborne dust sampling using filter loaded sampling heads with pumps are generally used for measurement. However, in some studies reservoir dust is collected and concentrations are expressed as weight units per gram or per m² with the latter reflecting the actual exposure. The methods used to quantify (1-3) β-D-glucan in environmental and occupational exposure assessment studies include the monoclonal ELISA methods, Fungitec G test and the LAL-based Glucatell assay. Although the ELISA methods are considerably cheaper than the LAL-based assay, they are significantly less sensitive, thus the two methods are not correlated. ELISA methods are also not available commercially. The challenge is to standardise the protocols since different extraction procedures and quantification methods are used.

3.3. Microbial volatile organic compounds (MVOCs): All animal facilities produce volatile organic compounds when microbes metabolise various organic substances found in these settings. Poultry litter can also produce excessive MVOCs from fungi species as a result of microbial biodegradation of the organic matter and feedstock. Several studies demonstrated that the emitted MVOCs’ pattern of fungi cultures is dependent on the fungal species and the substrate. MVOCs commonly emitted from poultry litter include alcohols, acids, sulphides and high levels of terpenes and ketones. The latter two concentrations exceeded the threshold limit values (TLVs) recommended by the American Conference of Governmental Industrial Hygienists (ACGIH) for several VOCs. Passive charcoal sorbent tubes are placed in ambient air for 8-24 h and the extracts are analysed for MVOCs using GC-MS according to that described by Matysik and colleagues.

4. Health risks associated with exposure to hazardous biological agents in poultry farms

Poultry workers have an increased incidence of respiratory symptoms and a decline in lung function related to exposure to organic dust (Table 2). The severity of occupational health problems in the poultry farms might be more influenced by the composition of the dust rather than the levels of airborne particles alone. Microorganisms represent less than 1% of airborne particles however, and are often linked with the negative health effects associated with the

"Dose-response relationships have not been established for most biological agents."
poultry industry. The extent to which they become hazardous to human health depends on the occupational context, the circumstances surrounding exposure (e.g., specific agent, dose and duration of exposure, concurrent exposures) and worker susceptibility (genetic predisposition, age and immunosuppression). Short-term exposure to biological agents may lead to acute respiratory effects and can occur minutes after entering the poultry house while longer-term exposure may be linked with impaired lung function. In addition, it has been recently recognised that low grade exposure to certain poultry antigens can stimulate the immune system, resulting in hypersensitivity reactions. The most common work-related symptoms that have been reported in poultry workers include acute cough, excess phlegm, eye irritation, chest tightness, shortness of breath, fatigue, nasal congestion, sneezing, wheezing, headache, nasal discharge, throat irritation, fever and muscle aches. Clinical disorders observed in poultry workers include occupational asthma or asthma-like syndrome, allergic and non-allergic rhinitis, hypersensitivity pneumonitis (Farmer’s lung), toxic pneumonitis and chronic bronchitis.

5. Dose-response relationship
Dose-response relationships have not been established for most biological agents. Moreover, the precise role of biological agents in the development or aggravation of symptoms and diseases is only poorly understood. In most situations, combined exposure to complex mixtures of toxins and allergens, as well as interactions with non-biological agents, occur in the workplace and a wide range of potential health effects have to be considered. However, it is difficult to determine which of the constituents primarily accounts for presumed health effects. Several studies have revealed a complex, dose-dependent, non-linear relationship between environmental exposure to some biological agents such as endotoxins, fungal spores and other pathogen-associated molecular patterns (PAMPs) and the outcome of immune responses.

6. Occupational exposure limits (OELs) for biological agents in poultry settings
It is within the scope of the Regulations for Hazardous Biological Agents of South Africa under the OHS Act, 1993 to determine and assess the risks that are posed by biological agents in the workplace. However, the large uncertainties in quantitative exposure assessments and the lack of established dose-effect relationships hamper the development of legal OELs and evaluating the perceived risk. Some health based recommended occupational exposure limits (HBROEL) have been proposed for certain biological agents to assist with decision-making and interpretation of measurement results. In the Netherlands, The Dutch Expert Committee on Occupational Standards recommends a HBROEL for airborne endotoxin of 50 EU/m³, however the level is currently under review. The diversity of biological agents potentially present in poultry settings, and their various health effects on individuals, makes it difficult to establish safe or unsafe levels. Furthermore, seasonal variability adds to the complexity of setting specific standards. The HBA Regulation does not include filamentous fungi and microbial metabolites possibly due to lack of supporting evidence that these agents can cause diseases at the time of its elaboration. Therefore more research focusing on the association between biological exposure and clinical symptoms should be a priority.

7. Exposure control and medical surveillance of workers to poultry dust
Guidelines are available for risk assessments of biological hazards, however, the assessment of biological risk is seriously hampered as neither standardised sampling and analytical methods nor
Legislated OELs are available.\textsuperscript{40,44,49,52} In addition, the assessment is further complicated by concurrent exposure to biological agents as mentioned above, which should be assessed individually.\textsuperscript{53}

Emphasis is also placed on enforcing good work practices as far as reasonably practicable (e.g. engineering controls, respirator use and personnel behaviour)\textsuperscript{9} which should result in reduction of risk of exposure as per legislative requirements. These would include:\textsuperscript{9}

- the introduction of manual work practices;
- maximise ventilation without compromising the welfare of birds;
- provide workers with suitable filtering respiratory protective equipment with appropriate fit;
- avoid disturbing the chickens and litter to minimise the generation of dust;
- reduce individual worker exposure through job rotation;

For these reasons, the complete range of airborne microorganisms may not be recognised and the true concentration of biological substances may be miscalculated.\textsuperscript{52} Research should therefore include the validation and standardisation of available methods to reduce inter-laboratory and exposure variability. Until then, total inhalable dust measurements (>10 mg/m\textsuperscript{3}) may provide some evidence of association to health effects.\textsuperscript{57}

Key to preventing and controlling microbial infections in poultry settings would be to ensure that biological contaminants fall within legal limits. However, the lack of stipulated OELs is a major hindrance to ‘compliance’. In South Africa, another hurdle is the definition of HBAs as stipulated in the HBA Regulation. Most major biological agent categories synonymous with the poultry industry such as fungi, arthropods (mites) and vegetable/plant proteins (grain) do not appear in

\textbf{"The assessment of biological risks is further complicated by concurrent exposure to biological agents..."}

- introduce "low dust" methods such as washing or vacuuming as opposed to portable blowers and compressed airlines; and
- enforce procedures of good work practices (e.g. workers’ training and risks associated with their duties).

It is also essential that employers carry out health surveillance. This should include pre-employment screening, questionnaire after employment to enquire about any developing symptoms and a confidential health record for each worker. Lung function testing may also be useful for assessing the respiratory health of workers.\textsuperscript{9,45}

8. Contemporary and emerging issues

This review highlights a need for research to develop better tools for the detection and measurement of biological agents which will enable proper exposure assessments. Current culture techniques are laborious and time consuming and many organisms are non-culturable. Therefore, non-culture methods (e.g. light scattering spectrometry, scanning electron microscopy, GC-MS and PCR) appear more reliable, however, experience with these methods is still generally limited.\textsuperscript{40} Moreover using other techniques such as PCR yield measurement errors, as the viability of microorganisms is undeterminable without additional laboratory analysis.\textsuperscript{52,54-56}
the Regulation’s classification system for biological agents. This limitation points to the need for the development of specific regulations dealing adequately and effectively with the omitted biological agents.27

The relationship between exposure to biological agents and health effects is complex, dose-dependent, and in many instances follow a non-linear relationship. Still controversial is the seemingly paradoxical nature of endotoxin as well as the synergistic or multiplicative effect between co-exposures. Further research may serve to improve our understanding of how such biological agents interact with the immune systems and the health implications thereof.

CONCLUSION

The risk of developing work-related respiratory symptoms and lung function impairment increases with increasing exposure to poultry dust. An understanding of the key factors that contribute to the emergence and spread of bioactive agents and disease intelligence is needed, despite the lack of well defined OELs to these agents. Important areas that require further research include dose-response relationships with regard to mixed exposures in poultry settings.

REFERENCES


