MANAGEMENT AND PRODUCTION

Potential contaminants and hazards in alternative chicken bedding materials and proposed guidance levels: a review

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ABSTRACT Bedding material or litter is an important requirement of meat chicken production which can influence bird welfare, health, and food safety. A substantial increase in demand and cost of chicken bedding has stimulated interest in alternative bedding sources worldwide. However, risks arising from the use of alternative bedding materials for raising meat chickens are currently unknown. Organic chemicals, elemental, and biological contaminants, as well as physical and management hazards need to be managed in litter to protect the health of chickens and consequently that of human consumers. This requires access to information on the transfer of contaminants from litter to food to inform risk profiles and assessments to guide litter risk management. In this review, contaminants and hazards of known and potential concern in alternative bedding are described and compared with existing standards for feed. The contaminants considered in this review include organic chemical contaminants (e.g., pesticides), elemental contaminants (e.g., arsenic, cadmium, and lead), biological contaminants (phytotoxins, mycotoxins, and microorganisms), physical hazards, and management hazards. Reference is made to scientific literature for acceptable levels of the above contaminants in chicken feed that can be used for guidance by those involved in selecting and using bedding materials.

INTRODUCTION

Current rearing systems for meat chicken production usually use bedding materials to absorb moisture from bird excreta and to increase bird welfare. The combination of bedding material and bird excreta is known as "litter". In this review, both bedding and litter will be used. Bedding materials traditionally used around the world are usually organic (e.g., wood shavings, sawdust, bark, rice hulls, peanut and nut hulls, straw, shredded paper, and peat), but some inorganic materials have also been used (e.g., sand) (reviewed by Watson and Wiedemann, 2018). A substantial increase in demand and cost of chicken bedding has stimulated interest in alternative bedding sources worldwide (Grimes et al., 2002; Villagra et al., 2011; Garces et al., 2017; Kheravii et al., 2017). A number of alternative bedding materials, derived from recycled materials from the wood and paper industries (e.g., recycled wood, dried paper sludge, and recycled cardboard), and by-products of crop industries (e.g., cereal crop residues, crop and nut hulls) have been proposed (Grimes et al., 2006; Garces et al., 2017; Watson et al., 2018; Fernandes et al., 2019).

To date, there has been a number of studies on potential hazards and contaminants regarding the use of spent chicken litter for land application (reviewed by Kyakuwaire et al., 2019). However, very few studies have investigated potential contaminants that are detrimental to animals and humans in bedding materials before their use, and those are restricted to recycled wood and paper and cardboard by-products (Beauchamp et al., 2002; Asari et al., 2004; Fernandes et al., 2019). There have been many recent examples of contamination of chicken meat and eggs because of chicken exposure to persistent organic pollutants through contaminated feed, housing materials, and litter in traditionally raised chickens (Bernard et al., 2002; Brambilla et al., 2009; Winkler, 2015; Piskorska-Pliszczynska et al., 2016). Alternative bedding materials with unknown properties could increase such risks. Litter material may also be associated with increase in the incidence of diseases (Arne et al., 2011) and physical injury to chickens (Garces et al., 2017). Therefore, the

bedding used can potentially have negative impacts not only on bird health and welfare but also on overall food safety as contaminants can be transferred to humans consuming chicken meat.

This article reviews knowledge regarding contaminants and management risks associated with chicken bedding materials, focusing on the Australian production system, to enable the selection and risk management of alternative bedding. Because of the lack of guidelines to assess the risk of various contaminants and hazards in alternative bedding materials, contaminants that may be present in conventional bedding materials, housing structures, and in poultry feed that are able to cause disease in chickens and/or to be transferred to chicken products were reviewed. Contaminant levels that cause adverse health effects in chickens and maximum permitted levels of contaminants in feedstuff were provided to aid selection of alternative bedding using a risk management approach.

METHODOLOGICAL APPROACH

To investigate possible contaminants in alternative litter materials, a survey of the available published peer-reviewed literature on contaminants in feed and litter was conducted during January 2020 through a bibliographic study using Agricola, Web of Science, and PubMed databases. Government guidelines on maximum residue of contaminants in poultry meat and feed (Food and Safety Australia and New Zealand [**FSANZ**], Australian Pesticides and Veterinary Drugs, European Commission Regulation, Codex Alimentarius Commission) were also reviewed. Maximum levels recommended in feedstuff in Australia reviewed by MacLachlan et al. (2013) were also consulted. The main classes of potential contaminants of alternative litter identified are listed below. Impacts of choice of bedding material on the poultry house environment were also identified.

(1) Organic chemical contaminants (e.g., organochlorines and organophosphates);
(2) Elemental contaminants (e.g., arsenic, cadmium, lead, and mercury);
(3) Biological contaminants (e.g., phytotoxins, mycotoxins, and microorganisms)
(4) Physical contaminants and hazards

Whenever available, the no observed adverse effect level and the lowest observed adverse effect level for specific contaminants in meat chickens were recorded. In their absence, values for other poultry species or relevant animal models were used. The potential primary uptake pathway was considered to be through ingestion, although absorption through inhalation or skin contact for some of the compounds investigated in this review is possible. Guidance levels for contaminants in feed that would not result in exceedances of the current regulatory standards for edible tissues of chicken and for chicken health were reviewed. The use of feed intake

reference values is likely to be conservative as meat chickens have shown a maximum litter consumption of 6% (Malone et al., 1983). The 6% ingestion rate is likely to be an overestimate as overall consumption tends to be lower as birds age, and certain litter materials have a much lower consumption rate (Malone et al., 1983; Grimes et al., 2002). When using the feed guidance levels, it is important to consider not only the dietary intake through complete feed but also other potential contamination sources such as litter, soil, and other chicken housing materials.

Organic Chemical Contaminants

This review focuses on toxic organic contaminants of high international profile. A summary of the organic chemical contaminants and toxicological guidance levels for chickens is shown in Table 1. Emerging chemicals that may pose a high risk to human health and risks that are yet to be identified (Muir and Howard, 2006; Kleter and Marvin, 2009; Silano and Silano, 2017) were not reviewed. Antimicrobials are out of the scope of this review.

Persistent organic pollutants Persistent organic pollutants (**POP**) are widely recognized as food contaminants that are lipophilic and resistant to environmental degradation and can bioaccumulate in food chains (reviewed by Guo et al., 2019). The levels of compounds considered of particular harm are subjected to the Stockholm Convention Treaty on Persistent Organic Pollutants (2001 and 2009) as priority substances for elimination or restriction of release worldwide.

Persistent organic pollutants of importance for poultry include organochlorine pesticides (**OCP**), dioxins and dioxin-like polychlorinated biphenyls (**dl-PCB**); nondioxin-like PCBs; brominated flame retardants; polyaromatic hydrocarbons (**PAH**), and perfluorinated compounds (perfluorooctane sulfonic acid [**PFOS**]) (Table 1). Most POP are halogenated and can have many chemical isoforms, known as congeners. Bioaccumulation depends on congener, animal species, and tissue of interest (reviewed by MacLachlan and Bhula, 2008; MacLachlan, 2011; MacLachlan et al., 2013). Usually, concentration of those contaminants do not cause health problems to poultry; however, their transfer to meat products and eggs is of particular concern.

There have been many reports of eggs and meat products with levels of POP above the regulatory limits because of contaminated litter and feed materials. For example, litter and feed can become contaminated by use of lime and clay materials such as kaolin (Malisch, 2000; Carvalhaes et al., 2002; Malisch, 2017), pentachlorophenol (**PCP**)-treated wood (Ryan et al., 1985; Llerena et al., 2003; Brambilla et al., 2009; Piskorska-Pliszczynska et al., 2016), poultry access to decaying insulant material used in the poultry house (Hansen et al., 1989; Winkler, 2015), and dioxin and PCB-contaminated oil used in feed (Bernard et al., 2002).

Table 1. Organic pesticides of importance to poultry. Possible adverse effects and toxicological guidance limits for dietary ingestion in chickens.

Compound	Use	Possible hazards	Recommended maximum level in total poultry diet (mg/kg DM)[1]	Maximum limits (mg/kg wet weight) in chicken meat fat[2]	Toxicological guidance values
OCP					
Aldrin and Dieldrin (Σ HHDN + HEOD)	Insecticide	Neurological symptoms, endocrine disruption, infertility and fetal malformation, diabetes, cancer (breast cancer, testicular, prostate, liver, and kidney cancer), reproductive problems, cardiovascular problems, high blood pressure, glucose intolerance, and obesity	0.01	0.2	Mean lethal dose 10–15 mg/kg BW in chickens in a long-term study (Arant, 1952)
Chlordane	Insecticide		0.01	0.2 (mammals, no value set for chickens)	NOAEL of 0.3 ppm diet per day in chickens. Mean lethal dose of 220-230 ppm diet (FAO/WHO, 1968)
Dichlorodiphenyltrichloroethane (DDT) (Σ p,p'-DDT + o,p'-DDT + p,p' DDE + p,p'-DDD)	Insecticide		0.05	5	No effect on hepatic microsomal protein on hens orally administered 40 mg/hen of technical-grade DDT for 5 d. No effect on liver weights or body weight in chickens fed 800 ppm p,p'-DDT for 2–6 wk. Ataxia and death was observed in chickens fed 1,600 p,p'-DDT ppm for 2–4 wk (ATSDR, 2002)
Endrin	Insecticide/Rodenticide		0.03	0.05	NOAEL of 1 ppm in feed in chickens. Mean lethal dose of approximately 2–4 ppm feed (EFSA, 2005b)
Heptachlor (Σ heptachlor + epoxide)	Insecticide		0.02	0.2	Chickens fed heptachlor up to 0.3 ppm diet for 8 wk had no adverse effect. The mean lethal dose 62.4 mg/kg BW (IPCS, 1984)
Hexachlorobenzene (HCB)	Fungicide		0.01	1	Chickens fed 100 HCB ppm for 6 mo had no adverse effect (Avrahami and Steele, 1972)
Hexachlorocyclohexane (other than γ-HCH)	Insecticide		0.02	0.3	Dietary NOAEL of 625 ppm day in laying chicken fed beta-HCH for 12 wk (IPCS, 1991a)
Lindane (γ-HCH)	Insecticide		0.1	0.7	Acute oral LD50 596.8 mg/kg BW, no death at 150 mg/kg/BW. NOEL 4 ppm diet for 27 d (macroscopic changes in the liver) but no increase in mortality up to 84 ppm (IPCS, 1991b)
Mirex	Insecticide/flame retardant		0.005	Not set	Chickens fed mirex at 10 ppm and above had changes in the liver (Davison et al., 1976)
Toxaphene	Pest control on cotton and other field crops and poultry		0.05 (mg/kg 12% moisture content) (EU, 2011a)	na	Chickens fed 100 ppm diet from day 1 to maturity had had increased mortality. Mean lethal dose in birds for a 5-day dietary study is between 538–828 ppm (FAO/UNEP, 2005)
PCB/BDE					

Polybrominated diphenyl ether (PBDE)	Flame retardant	Reproductive problems, cancer, endocrine disruption, liver injury, cardiovascular disease in animal models	na	na	No NOEL/LOEL established in hatched chicks (McKernan et al., 2009) nor other species
Polychlorinated biphenyls (PCB) (Σ congeners)	Heat exchange fluids, electrical transformers and capacitors, additives in paint, carbonless copy paper, and plastics, lime		0.05	0.2	Broiler breeder and leghorn hens who were fed diets containing 0, 20 and 50 ppm Aroclor 1242 for 1 wk experienced reduced hatchability (67.3 and 27.8% of controls, respectively) (Briggs and Harris, 1973). Feed consumption reduced at 20 ppm (Lillie et al., 1974)
Polybrominated biphenyls (PBB)			0	na	No adverse effects up to approximately 64 ppm in feed for several wk, reduced feed intake and weight gains above 75 ppm and food refusal above 640 ppm (IPCS, 1984)
Dioxin and Furan					
Dioxin (PCDDs/ PCDFs) + dl-PCBs (Σ TEQ)	By-product of high-temperature processes, pesticide production, chlorine bleaching of paper	High blood pressure, glucose intolerance, and disturbances in mental and motor development, cancer, diabetes, endocrine disruption	0.2 ng TEQ/kg DM	3 pg TEQ/g fat (EU, 2011b)	Chicken oral NOAEL for mortality 100 ppm day for a 21 d exposure and 6,250 ppm for single exposure. Oedema in chicken fed 1,000 pg/g BW for 21 d (Gatehouse, 2004). Maximum daily intake recommended 1.4 pg/g/day.
Polycyclic aromatic hydrocarbons (PAH) and PFAS					
Perfluorooctane sulfonic acid (PFOS)	Fire-fighting foam, insecticide, photoimaging, aviation hydraulic fluids	Toxicity toward mammals in subchronic repeated dose studies at low concentrations, as well as rat reproductive toxicity with mortality of pups occurring shortly after birth, carcinogenic, and respiratory disease	na	na	Quail NOAEL for bodyweight and feed consumption between 10 and 20 PFOS ppm. Mortality in levels higher than 50-150 mg PFOS ppm (Newsted et al., 2007)
PAH4: Sum of benzo(a)pyrene, benzo(a)anthracene, benzo(b) fluoranthene and chrysene	By-product of high temperature processes, de-inking paper sludge		Oils and fats (0.2 mg/kg) (GMP, 2018)	na	Chicken embryo median lethal dose was different for different PAH compounds, whereas toxicity was not tested in nonembryonic chickens (Franci et al., 2018)
Parathion	Pest management in pome and stone fruit, citrus, and cotton	Causes cholinesterase inhibition with symptoms ranging from fever to respiratory paralysis and death	na	Not set	Oral mean lethal single dose in quails is 6 mg/kg BW, and a 5-day dietary 238 ppm/day (Hill, 1992)
Methyl parathion			na	Not set	Hens injected a single dose of 1 mg/kg/BW subcutaneously became paralyzed 10–14 d after treatment (APVMA, 2011). Mean lethal dose for quails on a 5-day dietary challenge of 69 ppm/day (Hill, 1992)
Melamine	Melamine is a metabolite of cyromazine, a drug used to control flies in poultry flocks and plant crops.	At high doses melamine causes crystals or stones in the urinary tract with kidney damage	2.5 (EU, 2017)	No limit	Dietary mean lethal dose > 5,620 ppm for ducks and quails

Abbreviation: NOAEL, no observed adverse effect level; LOAEL: lowest observed adverse effect level.

[1]Maximum recommended values for feedstuff in Australia as revised by MacLachlan et al. (2013). When there was no recommendation in Australia, European Union references were used. na = not available.

[2]Maximum limits in Australia according to the FSANZ (2016a,b). No limit = No Australian standard applicable for the contaminant. The "as low as reasonably achievable" principle applies. Not set = No Australian standard has been set for the chemical in the edible matrix and any detection is a contravention of the Australia New Zealand Food Standards Code. na = not available.

Organochlorine pesticides. Organochlorine pesticides are among the main classes of POP in the environment (Guo et al., 2019). They were widely used worldwide for treating soil, plants, and timber against various insects. These pesticides are chlorinated hydrocarbons or organochlorines, and several of those are included in the Stockholm Convention such as aldrin, dieldrin, chlordane, DDT, heptachlor, hexabenzene, mirex, and toxaphene. Owing to their persistence, these residues remain in the environment up to decades. These OCP have mostly been banned for agricultural use globally and have been replaced by less persistent and more water-soluble pesticides that have lower potential to bioaccumulate (Guo et al., 2019).

Bans on their use were introduced in Australia in the late 1980s, after detection of dieldrin and heptachlor in Australian beef exported to the United States (Corrigan and Seneviratna, 1990). Studies monitoring OCP in chicken meat in Australia have shown a decline in detection of residues with no detection of OCP in chicken meat products since the 19th Australian Total Diet Study conducted in 2001 (FSANZ, 2011).

Dioxin and dl-PCB. Sources of dioxin (**PCDD/F**) and dl-PCB contamination for livestock have been recently comprehensibly reviewed (Malisch, 2017; Weber et al., 2018). Dietary exposure to dioxins has been shown to cause death and chick edema disease when a mixture of PCB contaminated with PCDD/F was accidentally added to fat used in animal feeds in Belgium (reviewed by Bernard et al., 2002). Clinical signs of this disease include dyspnea, reduced body weight gain, stunted growth, subcutaneous edema, pallor, and sudden death. Domestic chickens appear to be the most sensitive livestock to dioxins (USEPA, 1993). In a dietary study with 3-day-old white leghorn cockerels, edema was induced in chicks fed 1,000 or 10,000 pg TCDD/g body weight (**BW**) per day for 21 d and in chicks fed 10,000 or 100,000 pg hexaCDD/g BW per day. In another dietary exposure study, domestic chickens given a single dose of TCDD at 25,000 to 50,000 pg/g BW died within 12 to 21 d after treatment (USEPA, 1993).

Free-range chickens are particularly prone to environmental contamination and can rapidly transfer dioxins into eggs (Schuler et al., 1997; Weber et al., 2018). Stephens et al. (1995) used chickens as a model for foraging animals to determine the bioavailability of PCDD/F in contaminated soil. Steady-state concentrations were reached after 80 d of daily intake of 42 pg/g international toxic equivalents (low-exposure group) and 460 pg/g international toxic equivalents (high exposure group). The tissue distribution was congener-dependent with 5 to 30% intake excreted in eggs, 7 to 54% deposited in adipose tissue, and less than 1% in the liver. On a fat weight basis, the highest concentrations were observed in the liver. Results from this study indicate that animals foraging on soil containing low contamination levels may bioaccumulate these compounds to unacceptable levels (Stephens et al., 1995). Hoogenboom et al. (2006) further confirmed these results by feeding laying hens with different levels of dioxins and dioxin-like PCB for a period of 56 d. The feed containing 0.4 ng TEQ dioxins/kg (below the European Union [EU] limit of 0.75 ng TEQ/kg) resulted in levels in eggs just above the EU limit (2.5 pg TEQ/g fat). Dioxin-like and indicator PCB residues followed a pattern very similar to that of dioxins, demonstrating that consumption of feed or soil with even moderate levels of dioxins and dioxin-like PCBs, rapidly results in increased levels in eggs (Hoogenboom et al., 2006).

Chlorine-using or formerly chlorine-using industries, including those producing paper, magnesium, aluminum, or titanium dioxide, have a high PCDD/F emission potential. Sludge residues from paper production have led to significant PCDD/F contamination in soils (reviewed by Weber et al., 2018). A study evaluating the biotransfer of POP from dried paper sludge, recycled cardboard, and recycled wood shavings litter to chicken meat products found evidence of uptake of PCDD/F and PCB in meat but not in skin and liver from dried paper sludge (Fernandes et al., 2019). Other sources of dioxins may be related to contaminated soil used for free-range chicken farms or to feed produced from crops grown in proximity with industries with higher risk to contain PCB-related contaminants (Weber et al., 2018).

Wood from demolition and buildings are also likely to contain PCP and other PCCD/F contaminated products. Pentachlorophenol was widely used as a bactericide, fungicide, herbicide, defoliant, and wood preservative. Pentachlorophenol-treated wood was used extensively in animal housing and confinement facilities until the 1980s, when its use was limited and banned in Australia because of contamination by PCP with dioxins (UNEP, 2013). Polychlorinated biphenyl from stabilizers in fluorescent lights or home appliances, elastic sealant material, or paints may also contaminate demolition wood (Asari et al., 2004). In a study analyzing animal litter made of waste wood samples from 7 different plants in Japan, Asari et al. (2004) detected POP and inorganic toxic compounds such as arsenic, lead, copper, and chromium in most of the litter samples. In particular, coplanar PCB in 1 litter dust sample showed a high concentration level (1,200,000 pg/g, 240 pg TEQ/g), suggesting the potential for contamination from demolition waste.

Most of the poultry contamination with PCDD/F in recent years have been reported in chicken eggs, with potential to rapidly accumulate in chicken meat, primarily from exposure of chickens to treated wood. Ryan et al. (1985) described PCDD/F and PCB contamination in chicken meat because of exposure to PCP-wood shavings as litter material in Canada. Piskorska-Pliszczynska et al. (2016) described high levels of PCDD/F in free-range eggs from hens exposed to PCP-treated wood used as structural components in a 40-year-old poultry house in Poland. Similarly, Brambilla et al. (2009) described high levels of PCDD/F in eggs from hens exposed to contaminated PCP-wood shavings in Italy, and Winkler (2015) described high levels of PCDD/F

and PCB in organic-farmed eggs that had leached from corrugated asbestos-cement cover plates which covered roof and sidewalls of the poultry house in Germany. High levels of PCDD/F were detected in PCP-contaminated pine sawdust used as a carrier for choline chloride premix used as a feedstuff (Llerena et al., 2003). This same study showed the contamination of corn cob with PCDD/F after storage in the same silo that was previously used for the storage of the pine sawdust.

Polybromide diphenyl ethers and polychlorinate biphenyls. Brominated flame retardants are listed as POP under the Stockholm Convention, including poly-brominated diphenyl ethers (**PBDE**), polybrominated biphenyls, and hexabromocyclododecane (**HBCD**) (Weber et al., 2018). Those compounds are used as additive flame retardants for electronics, linings under carpets, chairs, mattresses, and sofas. Concern has been raised because of the occurrence of several chemical compounds in the environment, including feed and food, especially seafood and grasses (FSANZ, 2007; Schecter et al., 2008; Fernandes et al., 2016). This has led to bans on the production and use of certain formulations of PBDE (EFSA, 2012). Commercial Penta- and Octa-PBDE mixtures were banned in Australia in 2005, whereas HBCD was banned worldwide in 2013 (Drage et al., 2019).

Hansen et al. (1989) described the contamination of turkey meat with PCB from ceiling vapor seal/insulation which fell to the litter and was consumed by the turkeys in a farm in the US. Hiebl and Vetter (2007) described the detection of high concentrations of pentabromocyclododecene (2.0 and 3.6 mg/kg egg fat), a metabolite of HBCD in 2 out of 79 pooled eggs in Germany, although the cause of contamination was not ascertained.

Polyaromatic hydrocarbons and perfluoroalkyl compounds. PFAS are used in a variety of commercial, domestic, and industrial products including additives for the production of fluorinated polymers for paper coatings, metal plating, photography, and semiconductors, as well as in hydraulic fluids, firefighting foams, lubricants, adhesives, stain and soil repellents, pharmaceuticals, and insecticides. Two PFAS of concern in Australia and internationally are PFOS and perfluorooctanoic acid (**PFOA**) (PFAS Health Panel, 2018). In the 24th Australian Total Diet Study Phase 2, there were no detections for PFOA, and only 2 detections for PFOS out of 50 foods tested (fish fillets and beef sausage) (FSANZ, 2016a).

Food can be contaminated by PAH that are present in air, soil, or water or during food processing and cooking. These compounds are produced during combustion and pyrolysis processes such as coal or forest fires (Franci et al., 2018). The transfer and exposure of PAH/PFAS from soil to food animals have been demonstrated and reviewed showing that exposure from soil is a significant pathway (Weber et al., 2018).

Acute and chronic diet exposure of mallard and quails to PFOA resulted in decreased weight gain, increased liver mass, and slight reductions in egg fertility and hatchling survivability (Newsted et al., 2007). There are no studies on transference of PFOS to chicken meat. Chicken embryo median lethal dose was different for different PAH compounds, whereas toxicity was not tested in nonembryonic chickens (Franci et al., 2018).

Organophosphate pesticides Organophosphate pesticides have been used to control insect pests in agriculture and public health. These are generally acutely neurotoxic and have low persistence in the environment. In Australia, there are 30 organophosphate actives, 6 of them approved for public use (chlorpyrifos, diazinon, dichlorvos, fenthion, maldison, and omethoate). Parathion and parathion-methyl are currently licensed for restricted use. Parathion is licensed for use in citrus, apples, grapes, and pears, and parathion-methyl is mainly used in apple and pear crops (NRA, 2000; APVMA, 2011).

Because animals can degrade and excrete parathion and parathion-methyl metabolites within a short time, a risk from eating meat seems to be unlikely, and they are considered to not bioaccumulate (IPCS, 1992; IPCS, 1993). However, there may be an additional hazard from parathion-methyl bound to glucosides (IPCS, 1993), and maximum residues for parathion and parathion-methyl in mammalian meats and offal have been established in Australia (FSANZ, 2016b), but there are no limits set for poultry meats and offal.

An in vivo study of neurotoxicity using chickens, Soliman et al. (1986) observed that a dose of parathion at 2 mg/kg BW acutely poisoned the chickens, but they recovered from neurotypical signs in a day or 2. In studies presented for the registration of parathion-methyl in Australia, a preliminary neurotoxicity study determined the median lethal dose of parathion-methyl in chickens to be 215 mg/kg BW (NRA, 1997). This compound reached the highest concentration in plasma 2 to 4 h after the single dose and was rapidly eliminated from the blood with a half-life of about 3 h. The mean recovery of parathion methyl in excreta, pooled eggs, and edible organs was respectively 50.7, <0.1, and 2% (mainly kidney and liver), providing evidence that the parathion-methyl is excreted rapidly after acute exposure (NRA, 1997).

Melamine and cyromazine Melamine is used in the production of resins and has numerous industrial uses. It is also a metabolite of a pesticide called cyromazine that is used as a veterinary drug in the treatment of poultry feed to control diptera larvae in chicken manure, administered as a pour-on to prevent blow-fly strikes on sheep, and to control flies in crops in some countries including Australia. There is a withholding period of 3 d for meat chickens. In poultry, up to 10% of cyromazine might be metabolized to melamine (EFSA, 2010). Melamine became of regulatory interest following incidents of food and feed adulterated with this compound that resulted in illness and death of human infants and pet animals, primarily as a result of kidney damage (EFSA, 2010).

In Australia, the maximum residues for cyromazine in poultry meat is 0.05 mg/kg and 0.1 mg/kg in edible offal

(FSANZ, 2016b). A study on the tissue depletion profile of cyromazine in chickens followed by oral administration alone or in combination with melamine for a period of 14 d showed that the use of cyromazine as a feed additive either alone (5 or 10 mg/kg) or in combination with melamine (both agents at 5 mg/kg) do not produce unsafe residue levels in edible tissues after the withdrawal period (Rairat et al., 2017). This study showed that the highest concentration of cyromazine occurred in the liver but fell below detectable limits within 3 d following drug withdrawal from feed and that combined feeding of both compounds did not significantly alter cyromazine tissue levels. However, in shorter periods of withdraw, the levels in tissues may violate current regulatory limits. In a review of cyromazine by FAO (2007), a trial with meat chickens conducted by Alterburger in 1987 was described. Chickens were fed with a diet mixed with cyromazine at 5 and 50 ppm for 31 d. Tissues were collected 4 h after removal of the feed for analysis. At the 5 ppm treatment level, residues of cyromazine ranged from 0.04 to 0.09 mg/kg in breast muscle and from 0.05 to 0.10 mg/kg in liver. At the higher dose level, residues in muscle ranged from 0.52 to 0.71 mg/kg and in liver from 0.36 to 0.76 mg/kg.

Elemental Contaminants

Important nonessential metals and metalloids of concern for animal health are arsenic, cadmium, lead, and mercury because they are readily transferred through food chains (Adamse et al., 2017). These compounds can be found contaminating alternative bedding materials such as paper sludge (Beauchamp et al., 2002; Villagra et al., 2011) and in chromated copper arsenate–treated wood (Asari et al., 2004; Živkov Baloš et al., 2019). Other essential dietary metals such as copper can be toxic at high intake levels. A summary of the elemental contaminants and toxicological reference values for chickens is shown in Table 2.

Arsenic The environmental presence of arsenic (**As**) derives from both natural and anthropogenic sources (reviewed by EFSA, 2009b). Most industrially produced As originates from agricultural products, such as insecticides, herbicides, fungicides, algaecides, wood preservatives, and growth stimulators for plants and animals. Drinking water and ingestion of contaminated food are primary As exposure pathways to humans and animals (Živkov Baloš et al., 2019). Arsenic toxicity is species-dependent, and inorganic As (arsenite and arsenate) is more toxic than organic As (Nachman et al., 2013). However, maximum residues levels in feed and food are reported as total As without differentiating between various As forms (FSANZ, 2016b).

Organic As-based drugs, for example roxarsone, have been used in poultry production for decades to treat coccidiosis and improve feed conversion. In Australia, roxarsone has not been used by the chicken industry since 2012 (ACMF, 2018), and As-based feed additives are not allowed in the US and EU (EFSA, 2009b;

Nigra et al., 2017), although it is still legally used for chicken production in many countries (Hu et al., 2017).

Other potential sources of As exposure to chickens are contact with As residues from chromated copper arsenate–treated wood, feedstuffs of mineral and marine origin, and water (Asari et al., 2004; Adamse et al., 2017; Živkov Baloš et al., 2019). Toxic effects of As in poultry are manifested by a decrease in feed consumption, weight gain, egg production, and neurological signs. Toxic ranges of arsenite started at 44 ppm feed for laying hens that showed a 24% decrease in feed intake and 20% decrease in egg production (Chiou et al., 1997).

Arsenic bioaccumulates in liver, heart, and kidneys of poultry (Desheng and Niya, 2006; Gul Kazi et al., 2013; Hu et al., 2017). In an experiment with Japanese quail fed a diet supplemented with 50 ppm and 100 ppm 4-arsanilic acid and drinking water containing 0.008 mg/l As found that the concentration of As in drumstick and breast meat did not exceed 0.64 mg/kg of dry matter, whereas content in liver, heart, and kidneys was significantly higher, ranging from 0.81 to 2.82 mg/kg of dry matter, and the highest amounts were recorded in the liver (Desheng et al., 2006). In a study with 250 commercial meat chickens in Pakistan, concentrations of As in different chicken feeds were found in the range of 21.3 to 43.7 mg/kg. The concentration of As in liver (3.07–7.17 mg/kg), heart (2.11–6.36 mg/kg), and in leg and breast (2.19–5.92 mg/kg) were lower than manure (22.8–50.3 mg/kg), suggesting a potential of contamination of crops when poultry litter is used as a fertilizer.

Cadmium Cadmium (**Cd**) is a widespread environmental contaminant (reviewed by Jarup and Akesson, 2009). The major sources of Cd exposure are natural occurrence and various industrial and agricultural activities. Owing to concentration in the food chain and possessing an extremely long biological half-life of 10 to 30 yr, there is no margin of safety of exposure for the general population. Generally, forages, fish meal, peanuts, and sunflower meal contain high levels of Cd, whereas poultry meat has little contribution to human exposure (EFSA, 2004a,b,c).

Maximum safe dietary concentrations for livestock cannot be estimated because Cd disposition is significantly influenced by dietary interactions with zinc, copper, iron, and calcium (EFSA, 2004a,b,c). Leach et al. (1979) investigated the Cd content in tissues of meat chickens supplemented with 3, 12, and 48 ppm Cd in feed. All levels of Cd resulted in increased Cd in the kidney, whereas 12 and 48 ppm levels caused Cd increases in liver and muscle. In a study in laying hens, Sharma et al. (1979) evaluated the effects of 0.3, 1.9, and 13.1 ppm Cd in diets administered to the hens and found no accumulation of Cd occurred in eggs or bones. There were no treatment-related changes in the body weight, egg production, and gross or histopathological lesions.

Lead Concentrated lead (**Pb**) sources include Pb-based paint, Pb-arsenate crop sprays, batteries, alloys, and lead mine tailings cause contamination to the air, water, and soil and persist indefinitely (JECFA, 2000). Before 1970, paints containing high levels of Pb were used in

Table 2. Metal and metalloids of importance to poultry. Possible adverse effects and toxicological guidance limits for dietary ingestion in chickens.

Compound	Source	Clinical signs of toxicoses in poultry and humans	Recommended maximum level in total diet (mg/kg DM)[1]	EU feed maximum levels (mg/kg, 12% feed moisture)[2]	Maximum levels (mg/kg) in poultry meat (and liver)	Toxicological guidance values
Arsenic	Drinking water, pesticides, coccidiostatics, wood-preservatives	Vaso-oclusion, peripheral neuropathy, encephalopathy, compromises immune system, carcinogenic	0.2 (cattle, sheep, pigs)[2]	2 (EU, 2015)	0.02 (1.0) (FSANZ, 2001)	Reduced weight gain after 10 × daily doses of 100 mg hydroxydimethylarsine oxide/kg BW but no clinical signs after exposure to other arsenic compounds up to a daily dose of 250 mg/kg BW (EFSA, 2005a)
Cadmium	Battery pigments, natural emissions	Oxidative stress, nephrotoxic, hepatotoxic, reduced growth	1	0.5 (EU, 2013)	0.05 (1.25) (FSANZ, 2016a,b)	Diets with 12 and 48 ppm resulted in increases in the cadmium content of liver and muscle (EFSA, 2004b)
Copper	Wood preservatives, disinfectants, pesticides	Essential trace element, excess cooper induces oxidative stress resulting in kidney, liver, and gastrointestinal damage	200	Na	2 (50) (FSANZ, 2001)	Dietary cooper above 250 ppm may increase feed conversion rate, and cause severe oral and gastrointestinal erosions (EFSA, 2016)
Lead	Natural emissions, battery manufacturing, paints	Neurotoxicity, cardiovascular adverse effects, nephrotoxicity	5 (cattle, pig, sheep)[2]	5 (EU, 2017)	0.1 (0.5) (FSANZ, 2016a,b)	LOAEL of 1 ppm (EFSA, 2004c)
Mercury	Natural emissions, batteries, preservatives	Neurotoxicity, adverse renal, and pulmonary dysfunction	0.01 (cattle, pig, sheep)[2]	0.1 (EU, 2017)	0.01 (0.01) (FSANZ, 2001)	NOAEL 2.2 mg/kg feed for young chickens (EFSA, 2008a)

Abbreviation: LOAEL, lowest observed adverse effect level; NOAEL, no observed adverse effect level.

[1]Maximum recommended values for feedstuff in Australia as revised by MacLachlan et al. (2013). When there were no values recommended for chickens, species for which recommendation is given in parenthesis.

[2]na = not available.

Table 3. Mycotoxins and phytotoxins of importance in poultry.

Toxin	Source	Crop origin	Toxicity	Recommended maximum level in total poultry diet (mg/kg DM)[1]	Toxicological guidance values
Mycotoxins					
Aflatoxins (B1+B2+G1+G2)	Aspergillus sp.	Peanuts, corn, cottonseed	Hepatotoxic, carcinogenic, immune suppression	0.02	Detrimental effects on weight gain and feed efficiency were observed at 1 ppm feed inclusion for 5 wk (EFSA, 2004a)
Ochratoxin A	Aspergillus sp.	Cereals, coffee, fruit	Nephratoxic, carcinogenic, neurotoxic, immunotoxic	0.1	Reduction in feed intake, body weight, and feed efficiency and increased mortality were observed at 0.4 ppm feed inclusion from hatch to 5 wk of age (Battacone et al., 2010)
Fumonisins (B1+B2+B3)	Fusarium sp.	Wheat, corn, rice, barley, oats, sorghum	Hepatotoxic, nephrotoxic, protein synthesis inhibitor	30	NOAEL of 20 ppm feed. Decreased body weight and feed efficiency at 100 ppm fumonisin B1 feed for more than 21 d (EFSA, 2018)
Zearalenone	Fusarium sp.	Wheat, bran, corn	Oestrogenic	2	A LOAEL of 200 ppm per day and a NOAEL of 50 ppm (Knutsen et al., 2017)
Deoxynivalenol, nivalenol	Fusarium sp.	Corn, wheat, oats, barley, rice	Nausea, feed refusal, neurotoxic	2	Reduced body weight gain and increased water consumption at 2.5 ppm feed daily (Huff et al., 1986)
Ergots					
Rye ergots	Claviceps sp.	Rye	Ovarian regression, vasoconstriction on peripheral blood vessels, neurotoxin	2,000 (0.2%) as ergot or 4 mg alkaloids/kg DM	LOAEL corresponded to a total dietary EA content of 5.7 ppm for day 1 to 14 of life or 2.0 ppm feed from day 14 to 35 d. NOAEL of 2.49 ppm diet until day 14 of age, and 1.94 ppm diet until day 35 of age (Dänicke, 2017).
Sorghum ergot	Claviceps sp.	Sorghum		200 (0.02%) as ergot	
Ergot other than sorgum	Claviceps sp.	Wheat, barley, corn		20,000 (0.2%) as ergot or 6 mg alkaloids/kg DM	
Phytotoxin					
Gossypol	Natural phenol	Cotton	Respiratory distress, impaired body weight gain, anorexia, depression, and death	100	Based on growth in meat chickens, a NOAEL of 200 ppm feed of free gossypol. A LOAEL of 400 ppm feed based on increased feed conversion rate (EFSA, 2009a)
Theobromine	Natural alkaloid	Cacao, tea	Neurotoxicity, reproductive toxicity	300 (EU, 2011a)	In young chickens, a NOAEL of 260 and 1,100 ppm diet with depressed feed intake at higher doses. In older meat chickens, LOAEL of 950 ppm (EFSA, 2008b)
Cyanogenic compounds	Natural cyanide	Apricot kernels, almonds, cassava	Cytotoxic hypoxia and death	10 (EU, 2011a)	The level of 80 mg cyanide/kg exerts no adverse effects in growing broilers (EFSA, 2007)

Abbreviation: NOAEL, no observed adverse effect level; LOAEL, lowest observed adverse effect level.

[1]Maximum recommended values for feedstuff in Australia as revised by MacLachlan et al. (2013). When there was no recommendation in Australia, European Union references were used.

domestic and commercial buildings in Australia (MacLachlan et al., 2013).

Consumption of chips of Pb-based paint peeling from a chicken house was associated to acute poisoning of laying hens (Trampel et al., 2003), whereas chronic exposure to Pb-contaminated soil has been implicated in subclinical exposure of backyard flocks (Leibler et al., 2018; Mordarski et al., 2018). Clinical signs of acute Pb poisoning in chickens include muscle weakness, ataxia, and loss of appetite, followed by marked weight loss and eventual cessation of egg production. Young chickens are more susceptible than adult chickens (Salisbury et al., 1958).

Bakalli et al. (1995) studied the toxic effects of supplemental dietary sulfate or acetate Pb in feed of meat chickens from hatching to 42 d of age. Lead supplementation caused linear decreases in body weight gain starting with 1 ppm feed and significant negative effects on feed conversion ratios at 10 ppm feed. Lead additions to the diet resulted in a dose-related increase of Pb in blood, kidney, liver, and tibia, whereas higher dietary calcium (1.3%) reduced Pb in blood and liver.

Mercury Mercury (**Hg**) exists in the environment as elemental (metallic), inorganic, and organic (primarily methylmercury). Elemental and inorganic Hg have considerable emissions from natural sources and industrial plants and are deposited to soil, water, and sediments, where they can be transformed into methylmercury which bioaccumulates in the food chain (reviewed by EFSA, 2008a). The toxicity of Hg depends on its chemical form. Elemental Hg is volatile and mainly absorbed through the respiratory tract. Gastrointestinal absorption of inorganic Hg is in the 10 to 30% range and distributes mainly in the kidneys, causing renal damage. Methylmercury is readily absorbed in the gastrointestinal tract (>80%) and distributed to all tissues with the nervous system being the primary site of toxicity.

Administration of mercuric chloride in drinking water at levels of 5, 25, and 125 ppm in meat chicken cockerels from hatch until 35 d old did not depress growth, cause mortality, or increase feed conversion ratios, whereas doses of Hg of 250 ppm or greater caused toxic symptoms in young chicks (Parkhurst and Thaxton, 1973; Thaxton et al., 1973a; Thaxton and Parkhurst, 1973b). After 5 wk of treatment, the mortality rates were 2.5% for the doses lower than 250 ppm, 15% for the 250 ppm dose, and 87.5% for the 500 ppm dose.

Swensson and Ulfvarson (1969) showed that when 10-week-old cockerels were given wheat dressed with the different Hg compounds at a concentration of 80 ppm of wheat, the methylmercury group developed paralysis and disturbances in coordination in 2 wk and died within 3 wk. No adverse reactions were observed in cockerels fed mercury (II) nitrate, methoxyethyl mercury hydroxide, or phenyl mercury hydroxide for 3 wk. Birds fed 16 ppm Hg of dressed wheat had no clinical signs or death.

Copper Copper (**Cu**) is an essential trace element that plays an important role as a cofactor in numerous enzymatic reactions that are involved in energy metabolism, the antioxidant defense system, pigmentation, and maturity and stability of collagen and elastin. Humans and poultry are generally tolerant of high Cu intake (EFSA, 2016). Copper toxicosis causes high mortality, severe anemia, greenish excreta, gizzard erosions, and pale viscera.

Naturally occurring cases of Cu toxicity because of feed intake are rare in poultry, most often because of accidental overdoses of copper sulfate or other Cu sources (Malinak et al., 2014). Accidental acute poisoning has been described in 2-day-old turkeys placed on wood shaving bedding disinfected with copper sulfate (Giergiel et al., 2019).

Biological Contaminants

A risk associated with organic beddings is the potential of introduction of biological contaminants such as toxins from plants and mold or microbes (bacteria and yeast) and viruses.

Phytotoxins A summary of the phytotoxins of interest and toxicological guidance values in chickens is given in Table 3.

Phytotoxins from weed seeds. Crop residuals, such as linseed, sorghum, and wheat, may be contaminated by poisonous plants or seeds during harvest leading to carry-over to litter or feed. Human exposure from animal derived products seems to be low, especially in meat products, but can cause high mortality and decreased weight gain in poultry (EFSA, 2011a). Common weed seeds found in coarse grain feed in Australia have been reviewed by the Queensland Department of Agriculture and Fisheries (DAF, 2015). From the weeds toxic to chickens, castor oil plant (*Ricinus communis*) seeds contains ricin, a toxic glycoprotein that causes significantly reduced feed intake and weight gain and high mortality at a dose of 10 g/kg BW, and a single dose of approximately 1 g/kg BW of castor bean husk can cause poisoning in pullets (Okorie and Anugwa, 1987; EFSA, 2008b; Diarra and Seidavi, 2018).

Mexican poppy (*Argemone ochroleuca* and *Argemone mexicana*) contains isoquinoline alkaloids and can cause growth depression, edema, and death when fed at 1 and 3% diet to cockerels from hatch to 3 wk of age, although the concentration of seeds that cause loss of production may change according to the alkaloid concentration in the seed (Norton and O'Rourke, 1980).

Sesbania pea (*Sesbania* spp) contains toxic amino acids such as L-canavanine that causes weakness, depression, anorexia, diarrhea, ruffled feathers, and rapid loss of body weight. When male meat chickens were fed diets containing 0.10 to 2% ground *Sesbania macrocarpa* seeds from hatch to 21-day-old, inclusions of 1% or more caused significant reduction in body weight and feed consumption but no mortality (Flunker et al., 1990). A dietary dose of 1% extracts of *Sesbania drummondii* per kg/BW is lethal when given orally to chickens (Flory and Hébert, 1984).

Seeds containing pyrrolizidine alkaloid such as crotalaria (*Crotalaria spectabilis, Crotalaria retusa, Crotalaria pallida,* and others), Salvation Jane (*Echium plantageneum*), and potato weed (*Heliotropium europaeum*) cause loss of appetite, anemia, ascites, kidney damage, and darkened combs and wattles in chronic cases and sudden death in acute cases (Sippel, 1964). These plants are unpalatable, and poisoning occurs primarily when feed becomes contaminated during harvest (Sippel, 1964; Williams and Molyneux, 1987). Seeds that contain more than 1% of the pyrrolizidine alkaloids can cause acute poisoning, whereas seeds that contain less than 1% are toxic if consumed in sufficient amounts for prolonged periods (Norton and O'Rourke, 1979; Williams et al., 1987; Diaz et al., 2003). Pathological liver changes can be seen at an inclusion rate of pyrrolizidine alkaloid of 390 ppm (Eroksuz et al., 2008).

Cyanide. Cyanide is usually released on the hydrolysis of cyanogenic glycosides and can cause death in animals and humans when ingested rapidly because of its ability to instigate cytotoxic hypoxia (Kadiri and Asagba, 2019). Plant foods that contain cyanogenic glycosides in kernel and seeds include apricot, almond, peach, cherry, nectarine, and plum, leaves of sorghum, and roots of cassava (Jaszczak et al., 2017).

Wiemeyer et al. (1986) administered 6, 12, 24, and 48 mg/kg BW doses of reagent grade sodium cyanide to 3 hens each via gelatin capsule delivered to the proventriculus. Clinical signs for all doses commenced at 6 to 10 min postexposure. At a 6 mg/kg dose, clinical signs were relatively mild (panting, eye-blinking, salivation). The estimated median lethal dose was 21 mg/kg. The concentration of cyanide in blood ranged from 0.70 to 1.6 ppm, whereas the concentration in livers ranged from undetectable to a maximum of 0.56 ppm, 30 min after exposure.

Chronic exposure of meat chickens with 1, 2, and 3 ppm of feed or body weight for 12 wk led to accumulation of cyanide in kidneys and liver that was followed by histopathological degeneration and inflammation in those organs (Kadiri et al., 2019).

Elzubeir and Davis (1988) tested the effect of sodium nitroprusside as a source of dietary cyanide in chickens. Growth and food intake were depressed in a progressive manner as the dietary concentration of sodium nitroprusside was increased from 0 to 0.5 g/kg. In a subsequent study, the same authors showed that diets containing 0.3 g/kg of sodium nitroprusside depressed growth rate and food intake but not in diets containing 0.1 g/kg (Elzubeir and Davis, 1990).

Gossypol. Gossypol is a phenolic compound in cotton stems, leaves, seeds, and flower buds with higher concentration in seeds (*Gossypium* spp.) (reviewed by EFSA, 2009a; Gadelha et al., 2014). Cottonseeds are a byproduct of cotton that is used for animal feeding, and cotton by-products can be used as bedding. Acute poisoning with gossypol can cause respiratory distress, impaired body weight gain, anorexia, depression, and death (Gadelha et al., 2014). After ingestion most of the gossypol is excreted, with relatively smaller amounts retained in the liver, followed by the kidney, plasma and muscle, blood, and kidneys (Lyman et al., 1969; Gamboa et al., 2001a).

Henry et al. (2001) added purified gossypol at 0, 0.1, 0.2, and 0.4 g/kg total diet and fed to 1-day-old meat chicks for 20 d. At the highest dose of gossypol, the feed conversion ratio was higher compared with the other treatments. When chicks were fed gossypol at 0, 0.8, and 1.6 g/kg diet for 22 d, the highest dose of gossypol resulted in 28% mortality and liver toxicity. Both dietary levels of gossypol resulted in reduced feed intake and decreased body weight gain.

Gamboa et al. (2001b) found similar effects when feeding meat chickens 0, 7, 14, 21 and 28% cottonseed meal, corresponding to 0, 0.13, 0.26, 0.39 and 0.53 g/kg diet of free gossypol, from hatch to 21 d of age. The highest dose decreased feed conversion and body weight compared to the control treatment. The fermentation of the cottonseed meal prior to inclusion in meat chicken diets seem to ameliorate the deleterious effects on feed conversion (Jazi et al., 2017).

Theobromine. Theobromine is naturally present in the cacao tree, seeds, and shells (*Theobroma cacao*) (reviewed by EFSA, 2008d) that can be used as bedding. Cocoa husk meal, cocoa bean shell, and cocoa bean meal have been reported to contain 1.5 to 4.0, 8.0 to 16.9, and 20 to 33 g theobromine per kg material, respectively. Inclusion of cocoa bean meal above 15% total diet and cocoa shell at 6% resulted in reduced feed consumption and reduced weight gain (Day and Dilworth, 1984; Oduns and Longe, 1998).

Fungus and mycotoxins Fungus and the mycotoxins that they produce are frequently reported in the air, feed, and litter of poultry houses (Dennis and Gee, 1973; Greco et al., 2014; Skora et al., 2016), with litter being the main contributor to fungal contamination. Most fungi species that produce mycotoxins belong to the genera *Aspergillus, Penicillium,* and *Fusarium* which are common fungi genera in poultry houses (Viegas et al., 2012), with important health implications for exposed workers and birds (Gigli et al., 2005; Viegas et al., 2013). From those, *Aspergillus* spp. are able to cause economically important disease in meat chickens. Contamination of litter with fungi and mycotoxins is discussed below, and a summary of the toxicological guidance levels of mycotoxins is given on Table 3.

Aspergillus. *Aspergillus fumigatus,* specifically, is a major respiratory pathogen that causes acute severe respiratory distress associated with granulomatous airsacculitis, pneumonia, ascites, and high mortality and morbidity in young chicks following inhalation of spores (reviewed by Arne et al., 2011). Feed conversion and growth rate in recovering birds remain poor throughout the production cycle (Dyar et al., 1984). This fungus can cause severe disease in immunocompromised humans but has very limited pathogenicity in healthy individuals (Latgé, 1999).

Inadequate ventilation and dusty conditions increase the risk of bird exposure to aerosolized spores that easily sporulate in poor quality contaminated feedstuffs and

litter (Debey et al., 1995; Gigli et al., 2005; Wadud et al., 2012). In meat chicken farms free from aspergillosis, the concentration of *Aspergillus* spp. in the air varied from 10 to 10^4 CFU/m^3 (Arne et al., 2011; Viegas et al., 2014), and the concentration of mold spores in wood litter was in the order of 10^5/g dry litter (So et al., 1978). Dust generated from fresh application of aspergillus contaminated hardwood shavings (2.5×10^6 organisms/g litter) was implicated in high mortality rates in a turkey flock (Dyar et al., 1984). After treatment of the litter with nystatin and copper sulfate, the mold count reduced to 1×10^4 organisms/g litter, and mortality was reduced, but performance of the flock remained poor.

Use of *A. fumigatus*-contaminated sunflower shell litter was associated with a severe aspergillosis outbreak, resulting in a 25% mortality in a meat chicken flock (Zafra et al., 2008). Fresh sugarcane bagasse litter was associated with up to 90% mortality in 6 flocks of young chickens caused by the high moisture content of the litter that favored *A. fumigatus* sporulation and growth (Hutson, 1966). No subsequent outbreak was noticed after stored stacked bagasse was used as litter material in subsequent batches.

Mycotoxins. Mycotoxins can cause toxic responses with a significant impact on performance in animal production by inducing acute and/or long-term chronic effects. There are 6 major groups of toxins: aflatoxins, ochratoxins, citrinin, ergot alkaloids, patulin, and fusariotoxins. Regulatory limits or maximum tolerated levels guidelines in food and feed have only been established for a few mycotoxins from some of the major toxin groups (Guerre, 2016).

The aflatoxins were first characterized after the death of more than 100,000 turkey poults was traced to the consumption of a mold-contaminated peanut meal (reviewed by Bennett and Klich, 2003). Aflatoxins are produced by *Apergillus* spp. in warm and humid conditions (Guerre, 2016). Among the aflatoxins (B1, B2, G1, and G2), aflatoxin B1 is the most toxic, both for humans and animals, and is a potent carcinogen. Concentrations of aflatoxin B1 as little as 0.5 ppm total diet fed to meat chickens from hatch to 44-day-old significantly decreased weight gain, carcass yield, and breast yield compared with controls (Mota et al., 2019). In laying chicks, aflatoxin B1 administered in feed from day 8 to 6 wk of age had detrimental effects in weight gain and feed efficiency after 4 wk when included at 5 ppm of total diet and after 5 wk at 1 ppm (Ehrich et al., 1986). In a study feeding meat chickens aflatoxin at 0, 2.5, and 5 ppm from hatch to 3 wk of age, both concentrations of aflatoxin decreased body weight and concentrations of 5 ppm decreased feed efficiency and hemoglobin levels in blood (Pearson et al., 1990).

Ochratoxins are produced mainly by some toxigenic species of *Aspergillus* and *Penicillium* (Magan and Aldred, 2005). Battacone et al. (2010) reviewed the effects of ochratoxin A in livestock production. In poultry, this mycotoxin acts as a nephrotoxin, and the reduction in growth performance of meat chickens is positively related with the concentrations of ochratoxin in feed and with the length of exposure to the toxin. Huff et al. (1975) fed ochratoxin A (0, 0.5, 1, 2, 4, and 8 ppm of feed) to chicks from 1 d to 3 wk of age. Growth was inhibited at concentrations above 2 ppm, whereas the kidneys were enlarged at doses of 1 ppm and above. Reductions in feed intake, body weight, and feed efficiency were observed when chicks were fed diets containing 0.4 and 0.8 ppm of ochratoxins from hatch to 5 wk of age, with mortalities of 5 and 13%, respectively (Elaroussi et al., 2006).

In temperate regions, *Fusarium* spp. fumonisins are more frequent (Guerre, 2016). Fumonisins affect the liver and the immune system in poultry species (reviewed by EFSA, 2018). Decreased feed intake, body weight, and feed efficiency were observed when meat chickens were fed diets containing 100 ppm fumonisin B1 for more than 21 d (Rauber et al., 2013; Poersch et al., 2014).

Deoxynivalenol (**DON**) is one of several mycotoxins produced by certain *Fusarium* species that frequently infect corn, wheat, oats, barley, rice, and other grains in the field or during storage. DON affects animal and human health causing acute temporary nausea, vomiting, diarrhea, abdominal pain, headache, dizziness, and fever (reviewed by Sobrova et al., 2010). Acute DON mycotoxicosis rarely occurs in poultry flocks under normal conditions, but concentrations lower than 5 ppm DON diet can lower productivity, impair immunity, and increase susceptibility to infectious diseases (Awad et al., 2013). Lucke et al. (2017) included DON at 0, 2.5, 5, and 10 ppm in diet fed to meat chickens from day 1 up to 5 wk of age. All concentrations of DON significantly reduced body weight gain and increased the water consumption. The oral median lethal dose of DON is approximately 140/kg BW for day-old chicks (Huff et al., 1981).

Zearalenone is a mycotoxin produced by several *Fusarium* species (reviewed by EFSA, 2011b; Knutsen et al., 2017). It is commonly found in maize but can be found also in other crops such as wheat, barley, sorghum and rye and has estrogenic activity. However, in poultry, zearalenone is characterized by a low oral bioavailability and a rapid elimination (Knutsen et al., 2017) even when high doses of zearalenone (50 mg/kg BW per day) were administered to chickens for 7 d (Chi et al., 1980). In meat chickens, lymphocyte count was the only parameter influenced by zearalenone.

Ergot alkaloids are produced by a number of *Claviceps* species that grow parasitically in cereal grains such as rye, wheat, triticale, barley, oats, sorghum, corn, rice, and several grass species (Bennett et al., 2003). The sclerotia or "ergot bodies" produced by this fungus contains mixtures of compounds that are highly variable in their alkaloid content and composition. Therefore, tolerance to individual ergot alkaloids present in feed materials is inconsistent (Bailey et al., 1999; EFSA, 2005b). Tolerance to ergot sclerotia seems have been reported below 0.3% or higher than 0.8% of diet contamination. Concentrations of 0.4% rye ergot,

0.3% wheat ergot, and 1% sorghum ergot may be safe for meat chickens.

Bacterial Bacterial contamination of poultry, feedstuff, and its implications to animal and human health have been extensively reviewed (Hinton, 2000; Crump et al., 2002; EFSA, 2005a; EFSA, 2008c; EFSA, 2019; Maciorowski et al., 2007). Feedstuff may become colonized by pathogenic bacteria through use of manure as fertilizer in crops, dispersal of pathogens by insects and feral animals feeding on crops, or during storage (Crump et al., 2002). Survival of bacteria of importance to animal and human health will depend on the pH, moisture, temperature, and aerobic climate in which crops and feed are stored (Maciorowski et al., 2007). There is a limited number of pathogens that could contaminate feedstuff and forage, infect chickens, and then lead to disease in humans, *Salmonella enterica* being the most important of them (Corry et al., 2002; EFSA, 2019). Völkel et al. (2011) compared the impact of the type of litter on the detection of *Salmonella* through boots swabs over time in a single meat chicken house and found that litter material may influence salmonella burden in flocks. Wood shavings showed the highest *Salmonella* prevalence (3/6 positive samples), followed by peat (2/6) and corn silage (1/6), whereas none of the 6 chopped straw samples were positive.

Risk of transmission of other pathogens such as *Campylobacter* sp., pathogenic strains of *Escherichia coli*, *Mycobacterium* sp., *Listeria monocytogenes,* and *Clostridium* sp. appear to be negligible (Hinton, 2000; EFSA, 2008c). However, on-farm feed or litter contamination with those or other pathogens can occur in rodent infested farms (Backhans and Fellström, 2012). Pathogens may utilize sporulation cycles (*Clostridium perfringens*) or mechanisms to resist acid (*L. monocytogenes*) and/or desiccation (*E. coli*) to survive in stored animal feeds (Maciorowski et al., 2007).

Outbreaks of *Mycobacterium avium* subsp. *hominissuis*, an opportunistic pathogen for pigs and humans, have been associated with the use of contaminated peat and sawdust in pig farms (Matlova et al., 2004; Matlova et al., 2005; Agdestein et al., 2011; Álvarez et al., 2011; Johansen et al., 2014). In all cases, the disease was described only on pigs, but this could represent a potential health and safety risk for farm workers in which peat is used as bedding material.

Viral Avian influenza virus (**AIV**) and Newcastle disease virus (**NDV**) are zoonotic viruses that may be transmitted from wild birds to chickens through droppings contaminating feedstuff or water (Alexander et al., 1984).

The likelihood of feed contaminated with excreta of wild migratory birds to transmit highly pathogenic AIV has been recently assessed and determined to be very low (USDA, 2015). In experimentally contaminated litter material and excreta with different strains of AIV, highly pathogenic AIV remained infectious for 96 h in excreta and less than 60 h in litter, whereas low pathogenicity AIV persisted less than 24 h in the different substrates (Reis et al., 2012; Hauck et al., 2017). All isolates retained infectivity for 1 d in wood shavings and shavings plus peanut hulls litter types, whereas in wood shavings plus gypsum, viruses remained infective for up to 3 d (Reis et al., 2012).

Although natural transmission of NDV from feed contaminated with feral pigeons excreta to chickens has been reported once (Alexander et al., 1984), without some adaptation of the virus to chickens, transmission of NDV strains that infect wild life to commercial indoor chickens appears to be unlikely (Ferreira et al., 2019). However, transmission of NDV from wild birds to backyard chickens has been reported (Dimitrov et al., 2016). In contaminated litter from poultry houses, NDV can remain infectious from less than 48 h to 16 d (Bankowski and Reynolds, 1975; Kinde et al., 2004). In more recent studies evaluating the viability and infectivity of NDV in litter contaminated by birds vaccinated with high doses of NDV, there was no evidence of virus transmission when naïve birds were introduced 1 to 5 d after removal of the seeder birds (Islam et al., 2013; Voss-Rech et al., 2017). The same studies have shown that chickens exposed to contaminated litter were infected with chicken anemia virus, infectious bursal disease virus, and fowl adenovirus but not infectious bronchitis or Marek's disease virus (Islam et al., 2013; Voss-Rech et al., 2017).

Physical Hazards

Contact dermatitis lesions (breast and hock burn, footpad dermatitis) are an important welfare issue for the meat chicken industry that can lead to significant loss in profitability. Contact dermatitis is a condition of inflammation and necrotic lesions on the plantar surface of the footpads of meat chickens (footpad dermatitis), breast (breast burn) and hock (hock burn) caused by a combination of litter moisture and chemical burning effect of ammonia in litter (Harms et al., 1977; Shepherd and Fairchild, 2010; Taira et al., 2014).

Development of breast blisters (sternal bursitis) or contact dermatitis seem to be related to the meat chicken genotype (Allain et al., 2009). A study reported increased incidence of breast blisters when sand was used as litter compared to sawdust, paddy straw and rice husk (Anisuzzaman and Chowdhury, 1996). Wood chips are also related to increased breast blisters compared to shavings (Grimes et al., 2002).

Contact dermatitis conditions are associated with various management parameters, including poor litter conditions, season, and increased bird age (Menzies et al., 1998; Haslam et al., 2007; de Jong et al., 2012; Bassler et al., 2013; Kaukonen et al., 2016). Poor litter conditions occur when a high absorbance load is placed on litter, and this is affected by the type of litter, the dietary formulation, intestinal disease, type of drinkers, stocking density, and other environmental factors such as temperature and humidity in the chicken house (Ekstrand et al., 1997; Menzies et al., 1998; Meluzzi et al., 2008; de Jong et al., 2012; Swiatkiewicz et al., 2017). The moisture absorbing and releasing capacities

of litter material are important to avoid lesion formation.

Lower footpad dermatitis scores have been observed in wood shavings when compared with straw in meat chickens (Sirri et al., 2007; Meluzzi et al., 2008; Kyvsgaard et al., 2013). One explanation for this observation is that straw tends to have higher moisture content initially when compared with other materials such as pine shavings, rice hulls, and peanut hulls (Grimes et al., 2002).

Recycled paper products have been found, with proper management practices, to be as effective as pine shavings. There was no difference in the occurrence of contact dermatitis when birds were reared in cotton waste chips to pine shavings but there was more caking with the cotton waste products (Grimes et al., 2006). Depth of litter (wood shavings or straw) higher than 5 cm were associated with higher prevalence of footpad dermatitis (Ekstrand et al., 1997; Martrenchar et al., 2002).

However, another study comparing pine shavings, pine bark, chipped pine, mortar sand, chopped wheat straw, ground hardwood pallets, ground door filler, and cotton-gin trash, found that mortar sand and ground door filler had significantly lower incidence of footpad dermatitis than did the other treatments (Bilgili et al., 1999). Wheat stalks have been associated to higher mortality and breast blister scores compared to wood shavings, rice hulls and hazelnut husks (Sarica and Cam, 2000).

Other factors that may cause physical damage in birds are wood splinters (Grimes et al., 2002) and the presence of extraneous components such as nails and other metal pieces. Best practices in recycled wood processing recommend visual inspection for removal of plastic wraps, with nails magnetically removed during the chipping process (NSWEPA, 2012) to minimize such contaminants.

Impacts of Bedding Properties on the Poultry House Environment

Wet litter In general, bedding materials need to be very absorbent. This is probably a good criterion for organic materials but might not apply to inorganic materials such as polystyrene, sand, or clay (reviewed by Grimes et al., 2002). In addition to being absorbent, the litter material must have a reasonable drying time. Many paper products absorb moisture but do not dry out appropriately (Grimes et al., 2002).

Various materials have been examined for use as litter and are generally tested for moisture holding capacity and drying rate, caking, and bird performance (reviewed by Watson et al., 2018). The best-performing material in terms of bulk density, moisture holding capacity, and drying rate was pine shavings, followed by rice hulls, ground corncobs, stump chips, pine sawdust, bark and chips, pine bark, and clay (Grimes et al., 2002). Pine straw (long and chopped) and peanut hulls were not included in the final ranking. Pine straw was found to be not suitable for litter as it caked over quickly. When litter particle size was less than 2.5 cm, bird performance was similar in hay, bark, and wood chip.

There were no significant differences in performance of meat chickens reared to 49 d of age or in ammonia levels, litter pH, or litter moisture in wood shavings and wood fiber pellets (65 mm diameter), and pens with wood fiber pellets had less severe caking (Grimes et al., 2002). On the other hand, wood fiber by-product from paper manufacture has a high moisture content, leading to excessive caking.

Ammonia emissions The damaging effects of ammonia on both birds and workers are well documented, and it is recommended that in-house concentration should be kept below 25 ppm with the ideal concentration being below 10 ppm (Naseem and King, 2018). Australian welfare standards require ammonia to be kept below 15 ppm at chicken head height for chickens older than 7 d of age and below 10 ppm for younger chicks (Animal Health Australia, 2017). Even at low levels, workers can experience acute effects such as irritation to the upper respiratory tract, nose, and eyes (Naseem et al., 2018). In chickens, ammonia causes damage in the respiratory tract, including partial loss of tracheal cilia at a concentration of 25 ppm (Anderson et al., 1966) and increased susceptibility to bacterial and viral airborne infections (Anderson et al., 1966; Quarles and Kling, 1974; Oyetunde et al., 1978; Beker et al., 2004).

Ammonia emissions increase when temperature and moisture content in litter increases (Miles et al., 2011a; Miles et al., 2011b). A laboratory study comparing ammonia volatilization in wood shavings, rice hulls, sand, and vermiculate found that wood shavings and rice hulls emitted the least ammonia (Miles et al., 2011b). In pen trials with meat chickens, wheat straw had reduced ammonia volatilization compared with wood shavings, especially under drinkers, which tend to become wet (Tasistro et al., 2007). However, wheat straw also caused reduced weight gain and greater caking compared with wood shavings.

Dust Poultry dust, which is a mixture of aerosolized litter, excreta, feather dander, feed, microorganisms, spores, and endotoxins, is a known health hazard for workers and birds (Riddell et al., 1998; Viegas et al., 2013). The drier the litter the more dust is created in the poultry house; fogging of oil or pure water can decrease dust concentration (Ellen et al., 2000). Over the production cycle, moisture from excreta is added by the birds, and the dust concentration tends to decrease (Shepherd et al., 2017). Although there are many studies dedicated to the harmful effects and mitigation of poultry dust, there are few reports directly assessing the contribution of different bedding materials on dust production (McGovern et al., 1999; David et al., 2015). Bedding materials such as peat moss and clay produce more dust when compared with pine shavings, sawdust, peanut hulls, corn cobs, and rice hulls (Howes et al., 1967).

Managing and Mitigating Risks

The risk management process outlined in ISO 31000 (ISO, 2018) states that if an identified risk exceeds the

risk threshold, then risk treatment such as management or mitigation should be considered. If testing of a potential alternative bedding material confirmed that contaminant levels exceeded guidance values, suitable mitigation measures could be an option to reduce the level of risk. However, very few studies exist that demonstrate the effectiveness of mitigation measures for contaminants in fresh poultry bedding. A relatively simple approach could be to blend litter materials containing known levels of chemical and elemental contaminants with materials that have little or no similar contaminants to reduce the contaminants concentration to a level where the risk of its use can be mitigated. This mitigation approach would however be ineffective when dealing with biological and physical contamination. Owing to the lack of information on mitigation measures for contaminants in bedding materials, mitigation measures are proposed below based on laboratory studies of pathogens in vitro or testing done on used litter. Some of these strategies have been adopted at a commercial scale; however, others would need further assessment for their effectiveness and cost benefit.

Infectivity of AIV and NDV in litter has been show to diminish after a certain period of time (Bankowski et al., 1975; Kinde et al., 2004; Reis et al., 2012; Hauck et al., 2017). As such, withholding periods before bedding is applied to the poultry house could reduce the risk of viral contamination. Such a withholding period would require bedding to be stored away from potential sources of recontamination such as bird droppings. Traditional methods for virus inactivation such as heat treatment, shallow fermentation, or chemical treatment (Stephens and Spackman, 2017; Voss-Rech et al., 2017) could reduce the risk of viral contamination from poultry bedding. However, the difficulty of ensuring uniform application and exposure of large quantities of bedding material to each of these treatments could make them less feasible.

Several treatments are available to inhibit fungal growth and minimize the risk of fungal diseases and mycotoxins. For example, treatment of the litter with nystatin and copper sulfate has been shown to reduce levels of fungal contaminants (Dyar et al., 1984). The FAO (Suttajit, 1991) recommend several strategies for fungal growth inhibition in feedstuffs (gamma-irradiation, synthetic fungicides, organic acids, and their sodium salts among others) but place prime importance on drying and proper storage of materials (low humidity, low temperature, away from pests). Some mycotoxins have been shown to be detoxified to varying degrees by treatments such as organic solvents, heating and pressure treating, gamma irradiation, or chemical treatment including acetic acid, ammonia gas or ammonium salts, calcium hydroxide, hydrogen peroxide, and sodium bisulfite among others (Suttajit, 1991).

Several treatments have been proposed to reduce the load of foodborne bacterial pathogens (*Salmonella, E. coli, Campylobacter* and *Listeria*) in litter and feed such as heat treatment, Pascalization, high pressure processing, steam, windrowing, and chemical methods such as quicklime (Jeffrey et al., 1998; Stringfellow et al., 2010; Bello et al., 2014; Vaz et al., 2017; Voss-Rech et al., 2017).

Physical contaminants can be removed through a variety of means such as magnetic screening for discrete metal contaminants, visual inspection for plastic materials, and screening such as mechanical sieving for large contaminants or dusty/fine materials (NSWEPA, 2012). Air separation grading uses differences in particle shape and density to separate materials using blown air and could be used as an alternative form of material separation.

Recent reviews of litter treatments showed that several litter amendments are suitable for use in poultry houses to reduce litter moisture and hence ammonia generation (Cockerill et al., 2020; de Toledo et al., 2020).

CONCLUSION

The principal purpose of this review was to identify the key contaminants and hazards for poultry and human health risks associated with bedding materials. Sustainable sourcing and management of bedding for poultry production is a recognized issue within poultry industries in many countries. The use of alternative bedding has the potential to adversely affect the health and welfare of chickens, workers, and consumers of chicken meat. Organic and elemental contaminants can be transferred from litter to the meat and organs of meat chickens during the production cycle and cause disease to chickens or make the meat unsuitable for human consumption. The maximum guidance levels in the total diet for poultry and the toxicological levels based on published experimental data are provided for key contaminants, which can be used as a trigger for further investigation or mitigation if exceeded in potential bedding materials. To assess the level of potential risk posed by these hazards, guidance values can be used as part of a semiquantitative risk assessment process in accordance with ISO 31000 (ISO, 2018) and 31010 (IEC, 2019).

It is crucial to consider the consequences and likelihoods of certain risks when choosing to use alternative bedding for poultry production and to consider control options. As such, a risk assessment method based on the guidance values suggested in this article will assist the chicken meat industry in assessing the likely hazards in alternative bedding materials.

Future research could improve knowledge around the transfer of contaminants from bedding material to meat chicken tissue and potential impacts to bird health, as there are very limited studies in this area (Fernandes et al., 2019). Based on the limited studies published, there is currently no indication that alternative bedding materials such as recycled wood, and by-products of the paper industry would cause illness to chickens or that transference of compounds would be above the maximum permitted limits in edible tissues. However, it is important to consider that there could be variability in contamination in different batches of bedding

material (Asari et al., 2004), and additional studies to ascertain the contamination potential of bedding materials from different sources is required.

While this review has identified potential hazards in litter based on available experimental data, additional hazards may be identified which represent significant risk to the industry, and further work needs to be done to both identify novel risks and provides guidance values to underpin industry risk assessments.

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DISCLOSURES

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